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# (54) Title: NUCLEAR RECEPTOR LIGANDS AND LIGAND BINDING DOMAINS

#### (57) Abstract

The present invention provides new methods, particularly computational methods, and compositions for the generation of nuclear receptor synthetic ligands based on the three dimensional structure of nuclear receptors, particularly the thyroid receptor (herein referred to as "TR"). Also provided are crystals, nuclear receptor synthetic ligands, and related methods.

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# NUCLEAR RECEPTOR LIGANDS AND LIGAND BINDING DOMAINS

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# CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims the benefit of the following provisional applications: 10 United States Ser. No. 60/008,540 and 60/008,543, filed December 13, 1995, and Ser. No. 60/008,606, filed December 14, 1995. This application claims the benefit of the following U.S. patent application: United States Ser. No. 08/764,870, filed December 13, 1996.

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### **INTRODUCTION**

#### Technical Field

This invention relates to computational methods for designing ligands that bind to nuclear receptors, crystals of nuclear receptors, synthetic ligands of nuclear receptors and methods of using synthetic ligands.

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### Background

Nuclear receptors represent a superfamily of proteins that specifically bind a physiologically relevant small molecule, such as hormone or vitamin. As a result of a molecule binding to a nuclear receptor, the nuclear receptor changes the ability of a cell to transcribe DNA, i.e. nuclear receptors modulate the transcription of DNA, although they may have transcription independent actions. Unlike integral membrane receptors and membrane associated receptors, the nuclear receptors reside in either the cytoplasm or nucleus of eukaryotic cells. Thus, nuclear receptors comprise a class of intracellular, soluble ligand-regulated transcription factors.

Nuclear receptors include receptors for glucocorticoids (GRs), androgens (ARs), mineralocorticoids (MRs), progestins (PRs), estrogens (ERs), thyroid hormones (TRs), vitamin D (VDRs), retinoids (RARs and RXRs), peroxisomes (XPARs and PPARs) and icosanoids (IRs). The so called "orphan receptors" are also

part of the nuclear receptor superfamily, as they are structurally homologous to the classic nuclear receptors, such as steroid and thyroid receptors. To date, ligands have not been identified with orphan receptors but it is likely that small molecule ligands will be discovered in the near future for this class of transcription factors. Generally, nuclear receptors specifically bind physiologically relevant small molecules with high affinity and apparent Kd's are commonly in the 0.01 - 20 nM range, depending on the nuclear receptor/ligand pair.

Development of synthetic ligands that specifically bind to nuclear receptors has been largely guided by the trial and error method of drug design despite the importance of nuclear receptors in a myriad of physiological processes and medical conditions such as hypertension, inflammation, hormone dependent cancers (e.g. breast and prostate cancer), modulation of reproductive organ function, hyperthyroidism, hypercholesterolemia and obesity. Previously, new ligands specific for nuclear receptors were discovered in the absence of information on the three dimensional structure of a nuclear receptor with a bound ligand. Before the present invention, researchers were essentially discovering nuclear receptor ligands by probing in the dark and without the ability to visualize how the amino acids of a nuclear receptor held a ligand in its grasp.

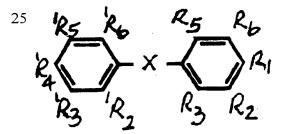
Consequently, it would be advantageous to devise methods and compositions 20 for reducing the time required to discover ligands to nuclear receptors, synthesize such compounds and administer such compounds to organisms to modulate physiological processes regulated by nuclear receptors.

#### SUMMARY OF THE INVENTION

The present invention provides for crystals of nuclear receptor ligand binding domains with a ligand bound to the ligand binding domain (LBD). The crystals of the present invention provide excellent atomic resolution of the amino acids that interact with nuclear receptor ligand, especially thyroid receptor ligands. The three dimensional model of a nuclear receptor LBD with a ligand bound reveals a previously unknown structure for nuclear receptors and shows that the ligand is bound in a water inaccessible binding cavity of the ligand binding domain of the nuclear receptor.

The present invention also provides for computational methods using three dimensional models of nuclear receptors that are based on crystals of nuclear receptor LBDs. Generally, the computational method of designing a nuclear receptor ligand determines which amino acid or amino acids of a nuclear receptor LBD interact with a chemical moiety (at least one) of the ligand using a three dimensional model of a crystallized protein comprising a nuclear receptor LBD with a bound ligand, and selecting a chemical modification (at least one) of the chemical moiety to produce a second chemical moiety with a structure that either decreases or increases an interaction between the interacting amino acid and the second chemical moiety compared to the interaction between the interacting amino acid and the corresponding 20 chemical moiety on the natural hormone.

Also provided is a method of modulating the activity of a nuclear receptor. The method can be *in vitro* or *in vivo*. The method comprises administering *in vitro* or *in vivo* a sufficient amount of a compound of the following formula:



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#### FORMULA I.

where the compound fits specially and preferentially into a nuclear hormone receptor LBD of interest. The method is exemplified by modulating the activity of a thyroid receptor (TR). For modulating TR activity, a compound of Formula I is employed

that fits spacially and preferentially into a TR ligand binding domain (TR LBD), including compounds specific for a TR LBD isoform of interest. Of particular interest are the TR LBD isoforms α (TR-α) and β (TR-β). Additional compounds of interest include derivatives of Formula I, such as those compounds having the biphenyl (φ-X-5 φ) or single phenyl (φ-X or X-φ) nucleus of Formula I and its corresponding substituent groups described herein. Compounds that are interatively designed using structural information gleaned from these compounds and which modulate nuclear hormone receptor activity also are of interest.

The present invention also includes a method for identifying a compound capable of selectively modulating the activity of a nuclear receptor. This aspect of the invention is exemplified by a method for identifying a compound capable of selectively modulating the activity of a TR isoform. The method comprises modeling test compounds that fit spacially and preferentially into a TR LBD isoform of interest using an atomic structural model of a TR LBD isoform bound to a test compound, screening the test compounds in a biological assay for TR isoform activity characterized by binding of a test compound to a TR LBD isoform, and identifying a test compound that selectively modulates the activity of a TR isoform. The compounds may be those of Formula I or derivatives thereof, including compounds having a biphenyl or single phenyl nucleus of Formula I.

Further included is a method for identifying agonist or antagonist ligands of a nuclear receptor using the atomic coordinates of a LBD in conjunction with a computerized modeling system. This aspect of the invention is exemplified by identifying a TR agonist or antagonist ligand by providing the atomic coordinates of a TR LBD to a computerized modeling system, modeling ligands which fit spacially into the TR LBD, and identifying in a biological assay for TR activity a ligand which increases or decreases TR activity. The compounds can be those of Formula I or derivatives thereof, including compounds having a biphenyl or single phenyl nucleus of Formula I.

Also provided is a method of identifying a compound that selectively 30 modulates the activity of one type of nuclear receptor compared to other nuclear hormone receptors. The method is exemplified by modeling test compounds which fit spacially into a TR LBD using an atomic structural model of a TR LBD, selecting a compound comprising conformationally constrained structural features that interact

with conformationally constrained residues of a TR LBD, and identifying in a biological assay for TR activity a compound that selectively binds to a TR LBD compared to other nuclear receptors. The conformationally constrained features involved in receptor-selective ligand binding can be identified by comparing atomic 5 models of receptor isoforms bound to the same and/or different ligands. The methods facilitate design and selection of compounds that have increased selectivity for a particular nuclear receptor. The compounds may be those of Formula I or derivatives thereof, including compounds having the biphenyl or single phenyl nucleus of Formula I.

Another aspect of the invention is a method for increasing the receptor 10 selectivity of a compound for a particular type of nuclear receptor. This involves the chemical modification of a substituent group of a compound of Formula I to generate compounds which have increased selectivity for one type of receptor. For example, chemical modification of a substituent group of the compound of Formula I can be 15 used to introduce additional constraints into a compound that modulates TR activity to increase its selectivity in vivo for TR-type receptors. Additional constraints also may The modified groups will preferably interact with a be added for stability. conformationally constrained structural feature of a TR LBD that is conserved among TR isoforms. A more preferred method comprises selecting compounds having 20 conformationally constrained groups that interact with conformationally constrained residues of a TR LBD conserved among TR isoforms. The compounds can be those of Formula I or derivatives thereof, including compounds having the biphenyl or single phenyl nucleus of Formula I.

The invention finds use in the selection and characterization of peptide, 25 peptidomimetic or synthetic compounds identified by the methods of the invention, particularly new lead compounds useful in treating disorders related to nuclear receptor-based deficiencies, including TR-related disorders. For TR-related disorders, the compounds and methods of the invention can be used to modulate TR activity by administering to a mammal in need thereof a sufficient amount of compound of 30 Formula I or derivative thereof that fits spacially and preferentially into a TR LBD.

# BRIEF DESCRIPTION OF THE DRAWINGS

- FIG. 1 is a diagram illustrating computational methods for designing ligands that interact with nuclear receptors of the nuclear receptor superfamily.
- FIG. 2 is a schematic representation of nuclear receptor structures, indicating 5 regions of homology within family members and functions of the various domains.
  - FIG. 3 shows the aligned amino acid sequences of the ligand binding domains of several members of the nuclear receptor superfamily.
- FIG. 4 is a ribbon drawing of the rat TR-α LBD with secondary structure elements labelled. The ligand (magenta) is depicted as a space-filling model. Alpha 10 helices and coil conformations are yellow, beta strands are blue.
  - FIG. 5 shows two cross-sections of a space-filling model of rat  $TR-\alpha$  exposing the ligand (magenta) tightly packed within the receptor.
- FIG. 6 is a schematic of the ligand binding cavity. Residues which interact with the ligand appear approximately at the site of interaction. Hydrogen bonds are shown as dashed lines between the bonding partners; distances for each bond are listed. Non-bonded contacts are shown as radial spokes which face toward interacting atoms.
- **FIG. 7** is the distribution of crystallographic temperature factors in the refined rat TR-I LBD. The distribution is represented as a color gradation ranging from less 20 than 15 (dark blue) to greater than 35 (yellow-green).
- FIG. 8 is a ribbon drawing of the rat TR-α LBD showing the c-terminal activation domain to ligand. Residues which comprise the c-terminal activation domain (Pro393-Phe405) are depicted as a stick representation. Hydrophobic residues, particularly Phe401 and Phe405 (blue) face inwards toward the ligand.

  25 Glu403 (red) projects outward into the solvent.
  - FIG. 9 is an electrostatic potential surface of the rat TR- $\alpha$  LBD, calculated using GRAPH. Negative electrostatic potential is red; positive electrostatic potential is blue. The c-terminal activation domain forms a largely hydrophobic (white). The Glu403 is presented as a singular patch of negative charge (red).
- FIG. 10 is a diagram comparing agonists and antagonists for several nuclear receptors.
  - FIG. 11 is the synthetic scheme for preparation of TS1, TS2, TS3, TS4 and TS5.

- FIG. 12 is the synthetic scheme for preparation of TS6 and TS7.
- FIG. 13 is the synthetic scheme for preparation of TS8.
- FIG. 14 is the synthetic scheme for preparation of TS10.
- FIG. 15 depicts the chemical structures of several TR ligands.
- FIG. 16 is a graph illustrating competition assays in which  $T_3$  and Triac compete with labeled  $T_3$  for binding to human TR-α or human TR-β.
  - FIG. 17 depicts a Scatchard analysis of labelled  $T_3$  binding to  $TR-\alpha$  and  $TR-\beta$ .
- FIG. 18 is a chart showing the effect of TS-10 on the transcriptional regulation of the DR4-ALP reporter gene in the presence or absence of T3 as assayed 10 in TRAFII reporter cells.
  - FIG. 19 is a chart showing the effect of TS-10 on the transcriptional regulation of the DR4-ALP reporter gene in the presence or absence of T3 as assayed in TRAF91 reporter cells.
- FIG. 20 is a chart showing the effect of TS-10 on the transcriptional 15 regulation of the DR4-ALP reporter gene in the presence or absence of T3 as assayed in HepG2, a liver reporter cell line.
  - FIG. 21 is a partial ribbon drawing of TR- $\alpha$  LBD with T3 in the ligand binding cavity. Selected interacting amino acids are labelled, including Ile221, Ile222 and Ser260, Ala263, Ile299 and Leu 276.
- FIG. 22 is a partial ribbon drawing of TR-α LBD with T3 and Dimit superimposed in the ligand binding cavity. Interactions with Ile221, Ile222, Ala260, Ile 299 and Leu276 are labelled.
- FIG. 23 is a partial ribbon drawing of TR-α LBD with T3, illustrating the three Arginine residues (Arg228, Arg262 and Arg 266 (dark stick figures)) of the polar pocket, three water molecules HOH502, HOH503 and HOH504, with hydrogen bonds indicated by dotted lines.
  - FIG. 24 is a partial ribbon drawing of TR-α LBD with Triac, illustrating the three Arginine residues (dark stick figures) of the polar pocket, water molecules (HOH503, HOH504 and HOH600), with hydrogen bonds indicated by dotted lines.
- FIG. 25 is a partial ribbon drawing of the TR-α LBD with T3 and Triac superimposed in the ligand binding cavity. The drawing shows several interacting amino acid residues in the polar pocket that remain unchanged whether T3 or Triac occupies the ligand binding cavity: Arg262, Asn179, HOH503 and HOH504, and

Ser277. Both Arg228 and Arg 266 occupy two different positions, depending on whether T3 or Triac is bound.

- FIG. 26A and 26B are stereochemical representations of the TR- $\alpha$  LBD with Dimit bound.
- FIG. 27 is a partial ribbon drawing of TR-β LBD with GC-1 in the ligand binding cavity. Amino acids Arg282, Arg316, Arg320, Asn 331 and His435 are labelled.
- **FIG. 28** is a partial ribbon drawing of TR-β LBD with Triac in the ligand binding cavity. Amino acids Arg282, Arg316, Arg320, Asn331 and His435 are 10 labelled.
  - FIG. 29 is a partial ribbon drawing of TR- $\beta$ LBD with GC-1 (Blue) overlayed with TR- $\alpha$  LBD with Dimit (Red) in the ligand binding cavities. Amino acids Arg228, Arg262, Arg266 and Ser277 (TR- $\alpha$  LBD), and Arg282, Arg316, Arg320 and Asn331 (TR- $\beta$  LBD) are labelled.
- FIG. 30 is a partial ribbon drawing of TR-β LBD with Triac (Blue) overlayed with TR-α LBD with Triac (Red) in the ligand binding cavities. Amino acids Arg228, Arg262, Arg266, Ser277 and His381 (TR-α LBD), and Arg282, Arg316, Arg320 and His435 (TR-β LBD) are labelled.
- FIG. 31 is a graph showing competition curves comparing wildtype TR-α and20 TR-β to a variant TR-β having a single amino acid substitution in the ligand binding domain.
  - FIG. 32 shows atomic numbering for thyronine-like ligands.

**APPENDIX 1** is an appendix of references.

**APPENDIX 2** is a chart of amino acids that interact with a TR ligand, for TR complexed with Dimit, Triac, IpBr2, T3 and GC-1.

APPENDIX 3 is a chart of atomic coordinates for the crystal of rat TR- $\alpha$  LBD complexed with Dimit.

APPENDIX 4 is a chart of atomic coordinates for the crystal of rat TR- $\alpha$  LBD complexed with Triac.

APPENDIX 5 is a chart of atomic coordinates for the crystal of rat TR-α LBD complexed with IpBr<sub>2</sub>.

APPENDIX 6 is a chart of atomic coordinates for the crystal of rat  $TR-\alpha$  LBD complexed with  $T_3$ .

APPENDIX 7 is a chart of atomic coordinates for the crystal of human TR- $\beta$  LBD complexed with Triac.

5 **APPENDIX 8** is a chart of atomic coordinates for the crystal of human TR-β-LBD complexed with GC-1.

#### DETAILED DESCRIPTION OF THE INVENTION

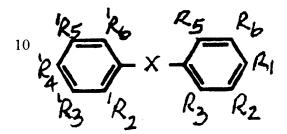
#### Introduction

The present invention provides new methods, particularly computational methods, and compositions for the generation of nuclear receptor synthetic ligands based on the three dimensional structure of nuclear receptors, particularly the thyroid receptor (herein referred to as "TR"). Previously, the lack of three dimensional structural information about the ligand binding domain of a nuclear receptor thwarted the field of nuclear receptor drug discovery, especially the absence of three dimensional structural information relating to a nuclear receptor with a ligand bound.

Described herein for the first time are crystals and three dimensional structural information from a nuclear receptor's ligand binding domain (LBD) with a ligand bound. The structure of the TR LBD complexed with 3,5,3'-triiodothyronine (T<sub>3</sub>), 20 3,5-dibromo-3'-isopropylthyronine (IpBr<sub>2</sub>), 3,5- dimethyl-3'-isopropylthyronine (Dimit), and 3,5,3'-triiodothyroacetic acid (Triac), 3,5-dimethyl-4-(4'-hydroxy-3'isopropylbenzyl)-phenoxy acetic acid (GC1) are exemplified. Such crystals offer superior resolution at the atomic level and the ability to visualize the coordination of nuclear receptor ligands by amino acids that comprise the LBD. The present 25 invention also provides computational methods for designing nuclear receptor synthetic ligands using such crystal and three dimensional structural information to generate synthetic ligands that modulate the conformational changes of a nuclear receptor's LBD. Such synthetic ligands can be designed using the computational methods described herein and shown, in part, in FIG. 1. These computational 30 methods are particularly useful in designing an antagonist or partial agonist to a nuclear receptor, wherein the antagonist or partial agonist has an extended moiety that prevents any one of a number of ligand-induced molecular events that alter the receptor's influence on the regulation of gene expression, such as preventing the

normal coordination of the activation domain observed for a naturally occurring ligand or other ligands that mimic the naturally occurring ligand, such as an agonist. As described herein, synthetic ligands of nuclear receptors will be useful in modulating nuclear receptor activity in a variety of medical conditions.

Of particular interest is use of such ligands in a method of modulating TR activity in a mammal by administering to a mammal in need thereof a sufficient amount of a compound of Formula I,



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where the compound fits spatially and preferentially into a TR LBD. By "fits spacially" is intended that the three-dimensional structure of a compound is accommodated geometrically by a cavity or pocket of a TR LBD. By "TR LBD" is intended a structural segment or segments of thyroid hormone receptor polypeptide 20 chain folded in such a way so as to give the proper geometry and amino acid residue configuration for ligand binding. This is the physical arrangement of protein atoms in three-dimensional space forming a ligand binding pocket or cavity. By "fits spacially and preferentially" is intended that a compound possesses a three-dimensional structure and conformation for selectively interacting with a TR LBD. Compounds of 25 interest also include derivatives of Formula I. By "derivatives of Formula I" is intended compounds that comprise at least a single phenyl scaffold (φ-X or X-φ) of the biphenyl scaffold  $(\phi - X - \phi)$  of Formula I which comprise the corresponding substituents of Formula I described herein. Compounds that are interatively designed using structural information gleaned from these compounds and which 30 modulate nuclear hormone receptor activity also are of interest. Preferred compounds of Formula I and its derivatives that fit spacially and preferentially into a TR LBD comprise the following substituents:

(i) an R1-substituent comprising an anionic group that interacts with a side chain nitrogen atom of an arginine corresponding to a residue from the group Arg228, Arg262, and Arg266 of human TR-α, and Arg282, Arg316 and Arg320 of human TR-β, where the anionic group is about 1.7-4.0Å from the nitrogen atom;

- 5 (ii) an R2-substituent comprising a hydrophobic or hydrophilic group that fits spacially into the TR LBD;
- (iii) an R3-substituent comprising a hydrophobic or hydrophilic group that interacts with a side chain atom of a serine, alanine and/or isoleucine corresponding to a residue from the group Ser260, Ala263 and Ile299 of human TR-α, and Ser314,
   10 Ala317 and Ile352 of human TR-β, where the hydrophobic or hydrophilic group is about 1.7-4.0Å from the side chain atom:
- (iv) an R5-substituent comprising a hydrophobic or hydrophilic group that interacts with a side chain atom of a phenylalanine and/or isoleucine corresponding to a residue from the group Phe218, Ile221 and Ile222 of human TR-α, and Phe272,
  15 Ile275 and Ile276 of human TR-β, where the hydrophobic or hydrophilic group is about 1.7-4.0Å from the side chain atom;
  - (v) an R6-substitutent comprising a hydrophobic or hydrophilic group that fits spacially into the TR LBD;
- (vi) an X-substituent comprising a hydrophobic or hydrophilic group that 20 interacts with a side chain atom of a leucine corresponding to a residue from the group Leu276 and Leu292 of human TR-α, and Leu 330 and Leu346 of human TR-β, where the hydrophobic or hydrophilic group is about 1.7-4.0Å from the side chain atom;
- (vii) an R2'-substituent comprising a hydrophobic or hydrophilic group that 25 fits spacially into the TR LBD;
- (viii) an R3'-substituent comprising a hydrophobic group that interacts with a side chain atom of a phenylalanine, glycine and/or methionine corresponding to a residue from the group Phe215, Gly290, and Met388 of human TR-α, and Phe269, Gly344, Met442 of human TR-β, where the hydrophobic group is about 1.7-4.0Å 30 from the side chain atom:
  - (ix) an R4'-substituent comprising an hydrogen bond donor or acceptor group that interacts with a side chain carbon or nitrogen atom of a histidine corresponding to residue His381 of human  $TR-\alpha$ , and His435 of human  $TR-\beta$ , where

the hydrogen bond donor or acceptor group is about 1.7-4.0Å from the side chain atom;

- (x) an R5'-substituent comprising a hydrophobic or hydrophilic group that fits spacially into the TR LBD;
- 5 (xi) and R6'-substituent comprising a hydrophobic or hydrophilic group that fits spacially into the TR LBD; and

where the compound is other than thyronine (T3), triiodothyronine (T4) or other thyronine-like compounds previously known and used in a TR treatment method, such as those referenced in Appendix I.

10 Examples of such substituents include the following: where  $R_1$  is

-O-CH<sub>2</sub>CO<sub>2</sub>H, -NHCH<sub>2</sub>CO<sub>2</sub>H, -CO<sub>2</sub>H, -CH<sub>2</sub>CO<sub>2</sub>H, -CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>H, -CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>H, -CH<sub>2</sub>CH[NHCOCH $\phi$ <sub>2</sub>]CO<sub>2</sub>H, -CH<sub>2</sub>CH[NHCO(CH<sub>2</sub>)<sub>15</sub>CH<sub>3</sub> ]CO<sub>2</sub>H, -CH<sub>2</sub>CH[NH-FMOC]CO<sub>2</sub>H,

-CH<sub>2</sub>CH[NH-tBOC]CO<sub>2</sub>H, or a carboxylate connected to the ring with a 0 to 3 carbon linker,

-PO<sub>3</sub>H<sub>2</sub>, -CH<sub>2</sub>PO<sub>3</sub>H<sub>2</sub>, -CH<sub>2</sub>CH<sub>2</sub>PO<sub>3</sub>H<sub>2</sub>, -CH<sub>2</sub>CHNH<sub>2</sub>PO<sub>3</sub>H<sub>2</sub>, -CH<sub>2</sub>CH[NHCOCH $\phi_2$ ]PO<sub>3</sub>H<sub>2</sub>, -CH<sub>2</sub>CH[NHCO(CH<sub>2</sub>)<sub>15</sub>CH<sub>3</sub>]PO<sub>3</sub>H<sub>2</sub>,

-CH<sub>2</sub>CH[NH-FMOC]PO<sub>3</sub>H<sub>2</sub>, -CH<sub>2</sub> CH[NH-tBOC]PO<sub>3</sub>H<sub>2</sub>, or a phosphate or phosphonate connected to the ring with a 0 to 3 carbon linker,

-SO<sub>3</sub>H, -CH<sub>2</sub>SO<sub>3</sub>H, -CH<sub>2</sub>CH<sub>2</sub>SO<sub>3</sub>H, -CH<sub>2</sub>CHNH<sub>2</sub>SO<sub>3</sub>H, -CH<sub>2</sub>CH[NHCOCH $\phi_2$ ]SO<sub>3</sub>H, -CH<sub>2</sub>CH[NHCO(CH<sub>2</sub>)<sub>15</sub>CH<sub>3</sub>]SO<sub>3</sub>H,

-CH<sub>2</sub>CH[NH-FMOC]SO<sub>3</sub>H, -CH<sub>2</sub> CH[NH-tBOC]SO<sub>3</sub>H, or a sulfate or sulfite connected to the ring with a 0 to 3 carbon linker, or acts as the functional equivalent of  $CH_2CH(NH_2)CO_2H$  of T3 in the molecular recognition domain

when bound to a TR, wherein R<sub>1</sub> can be optionally substituted with an amine,

where R2 is

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H, halogen, CF<sub>3</sub>, OH, NH<sub>2</sub>, SH, CH<sub>3</sub>, -Et, or acts as the functional equivalent of H in the molecular recognition domain when bound to a TR,

30 where R<sub>3</sub> is

-H, halogen, -CF<sub>3</sub>, -OH, -NH<sub>2</sub>, -N<sub>3</sub>, -SH, -CH<sub>3</sub>, -Et, or acts as the functional equivalent of I in the molecular recognition domain when bound to a TR, where  $R_5$  is

-H, halogen, -CF<sub>3</sub>, -OH, -NH<sub>2</sub>, -N<sub>3</sub>, -SH, -CH<sub>3</sub>, -Et, or acts as the functional equivalent of I in the molecular recognition domain when bound to a TR, and  $R_3$  can be identical to  $R_5$ ,

#### where R<sub>6</sub> is

5 -H, halogen, -CF<sub>3</sub>, -OH, -NH<sub>2</sub>, -SH, -CH<sub>3</sub>, or acts as the functional equivalent of H in the molecular recognition domain when bound to a TR, and R<sub>2</sub> can be identical to R<sub>6</sub>,

#### where R2' is

-H, halogen, -CF<sub>3</sub>, -OH, -NH<sub>2</sub>, -N<sub>3</sub>, -SH, -CH<sub>3</sub>, -Et, or acts as the functional equivalent of H in the molecular recognition domain when bound to a TR,

where R<sub>3</sub>' is any hydrophobic group, including

halogen, -CF<sub>3</sub>, -SH, alkyl, aryl, 5- or 6-membered heterocyclie, cyano, or acts as the functional equivalent of I in the molecular recognition domain when bound to a TR,

#### 15 where R<sub>4</sub>' is

-H, halogen, -CF<sub>3</sub>, -OH, -NH<sub>2</sub>, NH<sub>3</sub>, -N(CH<sub>3</sub>)<sub>3</sub>, carboxylate, phosphonate, phosphate or sulfate, -SH, -CH<sub>3</sub>, -Et, or akyl, aryl or 5- or 6-membered heterocyclic aromatic attached through urea or carbamate linkages to O or N or S at the R<sub>4</sub>' position, or acts as the functional equivalent of OH in the molecular recognition domain when bound to a TR,

#### where R<sub>5</sub>' is

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-H, -OH, -NH<sub>2</sub>, -N(CH<sub>3</sub>)<sub>2</sub> -SH -NH<sub>3</sub>, -N(CH<sub>3</sub>)<sub>3</sub>, carboxylate, phosphonate, phosphate, sulfate, branched or straight chain alkyl having 1 to 9 carbons, substituted or unsubstituted aryl, wherein said substituted aryl is substituted with halogen or 1 to 5 carbon alkyl and wherein said aryl is optionally connected to the ring by a -CH<sub>2</sub>-, aromatic heterocycle having 5 to 6 atoms, wherein said heterocycle may be substituted with one or more groups selected from -OH, -NH<sub>2</sub>, -SH, -NH<sub>3</sub>, -N(CH<sub>3</sub>)<sub>3</sub>, carboxylate, phosphonate, phosphate or sulfate, heteroalkyl, arylalkyl, heteroaryl alkyl, polyaromatic, or polyheteroaromatic, wherein said R<sub>5</sub>' may be substituted with polar or charged groups,

#### where R<sub>6</sub>' is

-H, halogen, -CF<sub>3</sub>, -OH, -NH<sub>2</sub>, -SH, -CH<sub>3</sub>, -Et, or acts as the functional equivalent of H in the molecular recognition domain when bound to a TR,

where X is

O, S, SO<sub>2</sub>, NH, NR<sub>7</sub>, CH<sub>2</sub>, CHR<sub>7</sub>, CR<sub>7</sub>R<sub>7</sub>, wherein R<sub>7</sub> is alkyl, aryl or 5- or 6-membered heterocyclic aromatic,

and where the TR LBD ligand has an apparent Kd for binding TR LBD of 1 TM or 5 less.

Of particular interest are the class of compounds according to Formula I having the following substituents: where R<sub>1</sub> is carboxylate, phosphonate, phosphate or sulfite and is connected to the ring with a 0 to 3 carbon linker, R<sub>2</sub> is H, R<sub>3</sub> is -I, -Br, or -CH<sub>3</sub>, R<sub>5</sub> is -I, -Br, or -CH<sub>3</sub>, R<sub>6</sub> is H, R<sub>2</sub>' is H, R<sub>3</sub>' is -I, -Br, -CH<sub>3</sub>, -iPr, -phenyl, 10 benzyl, or 5- or 6-membered ring heterocycles, R<sub>4</sub>' is -OH, -NH<sub>2</sub>, and -SH, R<sub>5</sub>' is -H, -OH, -NH<sub>2</sub>, -N(CH<sub>3</sub>)<sub>2</sub> -SH -NH<sub>3</sub>, -N(CH<sub>3</sub>)<sub>3</sub>, carboxylate, phosphonate, phosphate, sulfate, branched or straight chain alkyl having 1 to 9 carbons, substituted or unsubstituted aryl, wherein said substituted aryl is substituted with halogen or 1 to 5 carbon alkyl and wherein said aryl is optionally connected to the ring by a -CH<sub>2</sub>-, 15 aromatic heterocycle having 5 to 6 atoms, wherein said heterocycle may be substituted with one or more groups selected from -OH, -NH<sub>2</sub>, -SH, -NH<sub>3</sub>, -N(CH<sub>3</sub>)<sub>3</sub>, carboxylate, phosphonate, phosphate or sulfate, heteroalkyl, arylalkyl, heteroaryl alkyl, polyaromatic, or polyheteroaromatic, wherein said R<sub>5</sub>' may be substituted with polar or charged groups, and R<sub>6</sub>' is H.

The present invention also includes a method for identifying a compound 20 capable of selectively modulating the activity of a TR isoform. By "modulating" is intended increasing or decreasing activity of a TR. By "TR isoform" is intended TR proteins encoded by subtype and variant TR genes. This includes TR-α and TR-β isoforms encoded by different genes (e.g., thra and thrb) and variants of the same 25 genes (e.g., thrb1 and thrb2). The method comprises the steps of modeling test compounds that fit spacially and preferentially into a TR LBD isoform of interest using an atomic structural model of a TR LBD isoform bound to a test compound, screening the test compounds in a biological assay for TR isoform activity characterized by binding of a test compound to a TR LBD isoform, and identifying a 30 test compound that selectively modulates the activity of a TR isoform. "modeling" is intended quantitative and qualitative analysis of receptor-ligand structure/function based on three-dimensional structural information and receptorligand interaction models. This includes conventional numeric-based molecular

dynamic and energy minimization models, interactive computer graphic models, modified molecular mechanics models, distance geometry and other structure-based constraint models. Modeling is preferably performed using a computer and may be further optimized using known methods.

5 For selectively modulating activity of a TR isoform, such as TR-α or TR-β, a sufficient amount of a compound that fits spatially and preferentially into TR LBD isoform is provided *in vitro* or *in vivo* to achieve the desired end result. TR-α isoform selectivity can be accomplished with a compound comprising an anionic group that interacts with an oxygen or carbon of a serine residue corresponding to Ser277 of 10 human TR-α, where the anionic group is about 1.7-4.0Å from the side chain atom. TR-β isoform selectivity can be accomplished with a compound comprising an anionic group that interacts with the side chain nitrogen of an asparagine corresponding to Asn331 of human TR-β, where the anionic group is about 1.7-4.0Å from the side chain nitrogen atom.

The present invention further includes a method for identifying a TR agonist or antagonist ligand by providing the atomic coordinates of a TR LBD to a computerized modeling system, modeling ligands which fit spacially into the TR LBD, and identifying in a biological assay for TR activity a ligand which increases or decreases the activity of the TR.

The invention also involves a method for increasing receptor selectivity of a compound of Formula I or derivatives thereof for a TR-type receptor versus other nuclear receptors by selecting a compound that interacts with conformationally constrained residues of a TR LBD that are conserved among TR isoforms. "Conformationally constrained" is intended to refer to the three-dimensional structure of a chemical or moiety thereof having certain rotations about its bonds fixed by various local geometric and physical-chemical constraints. In designing and selecting compounds having increased specificity for TRs compared to other nuclear receptors, the following methods of the invention can be used. One method involves comparing atomic models of a first TR LBD isoform bound to a compound with a second TR LBD isoform bound to the same compound, identifying atoms of the TR LBD and compounds which interact, and designing or selecting a compound that interacts with TR LBD residues comprising a conformationally constrained structural feature that is conserved between the TR LBD isoforms. Another method relates to comparing a

first TR LBD complexed with a first compound to a second TR LBD complexed with a second compound having one or more different substituents compared to the first compound, identifying atoms of the TR LBD and compounds which interact, and designing or selecting compounds that interact with TR LBD residues comprising a 5 conformationally constrained structural feature that is conserved between the TR LBD isoforms. The methods also facilitate identification of structural and conformationally constrained interactions that are conserved between compounds that bind to a TR LBD. The methods are exemplified by comparing atomic models of a first TR LBD isoform complexed with a first compound of Formula I to a second TR LBD isoform 10 complexed with the first compound, or a second compound of Formula I having different substituents than the first compound. For example, a TR-α LBD bound to a natural hormone such as T3 is compared to a TR-β LBD bound to an organic thyronine-like compound such as GC-1. Conserved contacts are identified which are made between atoms of the different compounds and atoms of the TR LBDs, and the 15 fiducial and adjustable components identified. Compounds selective for TR are identified in a biological assay for TR activity that assays for selective binding to a TR and/or TR LBD compared to other nuclear receptors. Conventional assays for TR and other nuclear receptors may be conducted in parallel or serially, including those assays described herein. Automatable methods are preferred. The methods facilitate 20 design and selection of compounds comprising cyclic carbon and substituent atoms that interact with a constrained side chain and/or main chain atom of a TR LBD residue.

In another aspect of the invention, the methods described herein are useful for selecting peptides, peptidomimetics or synthetic molecules that modulate TR activity.

25 Methods of the invention also find use in characterizing structure/function relationships of natural and synthetic TR-ligands. Molecules of particular interest are new thyronine-like compounds other than T3, T4 and other thyronine-like compounds previously known and used for treating TR-related disorders. New compounds of the invention include those which bind to a TR LBD isoform with greater affinity than T3 or T4 and those which exhibit isoform-specific binding affinity.

#### APPLICABILITY TO NUCLEAR RECEPTORS

The present invention, particularly the computational methods, can be used to design drugs for a variety of nuclear receptors, such as receptors for glucocorticoids (GRs), androgens (ARs), mineralocorticoids (MRs), progestins (PRs), estrogens 5 (ERs), thyroid hormones (TRs), vitamin D (VDRs), retinoid (RARs and RXRs), icosanoid (IRs), and peroxisomes (XPARS and peroxisomal proliferators (PPAP)). The present invention can also be applied to the "orphan receptors," as they are structurally homologous in terms of modular domains and primary structure to classic nuclear receptors, such as steroid and thyroid receptors. The amino acid homologies 10 of orphan receptors with other nuclear receptors ranges from very low (<15%) to in the range of 35% when compared to rat RARI and human TR-β receptors, for example. In addition, as is revealed by the X-ray crystallographic structure of the TR and structural analysis disclosed herein, the overall folding of liganded superfamily members is likely to be similar. Although ligands have not been identified with 15 orphan receptors, once such ligands are identified one skilled in the art will be able to apply the present invention to the design and use of such ligands, as their overall structural modular motif will be similar to other nuclear receptors described herein.

## Modular Functional Domains Of Nuclear receptors

- The present invention will usually be applicable to all nuclear receptors, as discussed herein, in part, to the patterns of nuclear receptor activation, structure and modulation that have emerged as a consequence of determining the three dimensional structures of nuclear receptors with different ligands bound, notably the three dimensional structures or crystallized protein structure of the ligand binding domains for TR-α and TR-β. Proteins of the nuclear receptor superfamily display substantial regions of amino acid homology, as described herein and known in the art see **FIG. 2**. Members of this family display an overall structural motif of three modular domains (which is similar to the TR three modular domain motif):
  - 1) a variable amino-terminal domain;
- 30 2) a highly conserved DNA-binding domain (DBD); and
  - 3) a less conserved carboxyl-terminal LBD.

The modularity of this superfamily permits different domains of each protein to separately accomplish different functions, although the domains can influence each

other. The separate function of a domain is usually preserved when a particular domain is isolated from the remainder of the protein. Using conventional protein chemistry techniques a modular domain can sometimes be separated from the parent protein. Using conventional molecular biology techniques each domain can usually 5 be separately expressed with its original function intact or chimerics of two different nuclear receptors can be constructed, wherein the chimerics retain the properties of the individual functional domains of the respective nuclear receptors from which the chimerics were generated.

FIG. 2 provides a schematic representation of family member structures, 10 indicating regions of homology within family members and functions of the various domains.

#### Amino Terminal Domain

The amino terminal domain is the least conserved of the three domains and varies markedly in size among nuclear receptor superfamily members. For example, this domain contains 24 amino acids in the VDR and 603 amino acids in the MR. This domain is involved in transcriptional activation and in some cases its uniqueness may dictate selective receptor-DNA binding and activation of target genes by specific receptor isoforms. This domain can display synergistic and antagonistic interactions with the domains of the LBD. For example, studies with mutated and/or deleted receptors show positive cooperativity of the amino and carboxy terminal domains. In some cases, deletion of either of these domains will abolish the receptor's transcriptional activation functions.

#### 25 DNA-Binding Domain

The DBD is the most conserved structure in the nuclear receptor superfamily. It usually contains about 70 amino acids that fold into two zinc finger motifs, wherein a zinc ion coordinates four cysteines. DBDs contain two perpendicularly oriented I-helixes that extend from the base of the first and second zinc fingers. The two zinc 30 fingers function in concert along with non-zinc finger residues to direct nuclear receptors to specific target sites on DNA and to align receptor homodimer or heterodimer interfaces. Various amino acids in DBD influence spacing between two half-sites (usually comprised of six nucleotides) for receptor dimer binding. For

example, GR subfamily and ER homodimers bind to half-sites spaced by three nucleotides and oriented as palindromes. The optimal spacings facilitate cooperative interactions between DBDs, and D box residues are part of the dimerization interface. Other regions of the DBD facilitate DNA-protein and protein-protein interactions required for RXR homodimerization and heterodimerization on direct repeat elements.

The LBD may influence the DNA binding of the DBD, and the influence can also be regulated by ligand binding. For example, TR ligand binding influences the degree to which a TR binds to DNA as a monomer or dimer. Such dimerization also depends on the spacing and orientation of the DNA half sites. The receptors also can interact with other proteins and function to regulate gene expression.

The nuclear receptor superfamily has been subdivided into two subfamilies: 1) GR (GR, AR, MR and PR) and 2) TR (TR, VDR, RAR, RXR, and most orphan receptors) on the basis of DBD structures, interactions with heat shock proteins (hsp), and ability to form heterodimers. GR subgroup members are tightly bound by hsp in the absence of ligand, dimerize following ligand binding and dissociation of hsp, and show homology in the DNA half sites to which they bind. These half sites also tend to be arranged as palindromes. TR subgroup members tend to be bound to DNA or other chromatin molecules when unliganded, can bind to DNA as monomers and dimers, but tend to form heterodimers, and bind DNA elements with a variety of orientations and spacings of the half sites, and also show homology with respect to the nucleotide sequences of the half sites. By this classification, ER does not belong to either subfamily, since it resembles the GR subfamily in hsp interactions, and the TR subfamily in nuclear localization and DNA-binding properties.

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# Ligand Binding Domain

The LBD is the second most highly conserved domain in these receptors. Whereas integrity of several different LBD sub-domains is important for ligand binding, truncated molecules containing only the LBD retain normal ligand-binding activity. This domain also participates in other functions, including dimerization, nuclear translocation and transcriptional activation, as described herein. Importantly, this domain binds the ligand and undergoes ligand-induced conformational changes as detailed herein.

Most members of the superfamily, including orphan receptors, possess at least two transcription activation subdomains, one of which is constitutive and resides in the amino terminal domain (AF-1), and the other of which (AF-2 (also referenced as TAU 4)) resides in the ligand-binding domain whose activity is regulated by binding 5 of an agonist ligand. The function of AF-2 requires an activation domain (also called transactivation domain) that is highly conserved among the receptor superfamily (approximately amino acids 1005 to 1022). Most LBDs contain an activation domain. Some mutations in this domain abolish AF-2 function, but leave ligand binding and other functions unaffected. Ligand binding allows the activation domain to serve as 10 an interaction site for essential co-activator proteins that function to stimulate (or in some cases, inhibit) transcription.

For example, Shibata, H., et al. (Recent Progress in Hormone Res. 52:141-164 (1997)) has reviewed the role of co-activators and co-repressors in steroid/thyroid hormone receptor systems. Steroid receptor co-activator-one (SRC-1) appears to be a 15 general co-activator for all AF-2 domain containing receptors tested. SRC-1 enhances transactivation of steroid hormone-dependent target genes. Other putative coactivators have been reported, including the SRC-1 related proteins, TIF-2 and GRIP-1, and other putative unrelated co-activators such as ARA-70, Trip 1, RIP-140, and TIF-1. In addition another co-activator CREB-binding protein (CBP) has been shown 20 to enhance receptor-dependent target gene transcription. CBP and SRC-1 interact and synergistically enhance trancriptional activation by the ER and PR. A ternary complex of CBP, SRC-1, and liganded receptors-may form to increase the rate of hormone-responsive gene transcription. Co-repressors, such as SMRT and N-CoR, for TR and RAR, have been identified that also contribute to the silencing function of 25 unliganded TR. The unliganded TR and RAR have been shown to inhibit basal promoter activity; this silencing of target gene transcription by unliganded receptors is mediated by these co-repressors. The collective data suggests that upon binding of agonist, the receptor changes its conformation in the ligand-binding domain that enables recruitment of co-activators, which allows the receptor to interact with the 30 basal transcriptional machinery more efficiently and to activate transcription. In contrast, binding of antagonists induces a different conformational change in the receptor. Although some antagonist-bound receptors can dimerize and bind to their cognate DNA elements, they fail to dislodge the associated co-repressors, which results in a nonproductive interaction with the basal transcriptional machinery.

Similarly, the TR and RAR associate with co-repressors in the absence of ligand, thereby resulting in a negative interaction with the transcriptional machinery that silences target gene expression. In the case of mixed agonist/antagonists, such as 4-hydroxytamoxifen, activation of gene transcription may depend on the relative ratio of co-activators and co-repressors in the cell or cell-specific factors that determine the relative agonistic or antagonistic potential of different compounds. These co-activators and co-repressors appear to act as an accelerator and/or a brake that modulates transcriptional regulation of hormone-responsive target gene expression.

The carboxy-terminal activation subdomain, as described herein is in close three dimensional proximity in the LBD to the ligand, so as to allow for ligands bound to the LBD to coordinate (or interact) with amino acid(s) in the activation subdomain. As described herein, the LBD of a nuclear receptor can be expressed, crystallized, its three dimensional structure determined with a ligand bound (either using crystal data from the same receptor or a different receptor or a combination thereof), and computational methods used to design ligands to its LBD, including ligands that contain an extension moiety that coordinates the activation domain of the nuclear receptor.

Once a computationally designed ligand (CDL) is synthesized as described herein and known in the art, it can be tested using assays to establish its activity as an 20 agonist, partial agonist or antagonist, and affinity, as described herein. After such testing, the CDLs can be further refined by generating LBD crystals with a CDL bound to the LBD. The structure of the CDL can then be further refined using the chemical modification methods described herein for three dimensional models to improve the activity or affinity of the CDL and make second generation CDLs with 25 improved properties, such as that of a super agonist or antagonist described herein. Agonist and antagonist ligands also can be selected that modulate nuclear receptor responsive gene transcription through altering the interaction of co-activators and corepressors with their cognate nuclear hormone receptor. For example, CDL agonists can be selected that block or dissociate the co-repressor from interaction with the 30 receptor, and/or which promote binding or association of the co-activator. CDL antagonists can be selected that block co-activator interaction and/or promote corepressor interaction with the target receptor. Selection can be done in binding assays that screen for CDLs having the desired agonist or antagonist properties. Suitable assays for such screening are described herein and in Shibata, H., et al. (Recent Prog.

Horm. Res. 52:141-164 (1997)); Tagami, T., et al. (Mol. Cell Biol. 17(5):2642-2648 (1997)); Zhu, XG., et al. (J. Biol. Chem. 272(14):9048-9054 (1997)); Lin, B.C., et al. (Mol. Cell Biol. 17(10):6131-6138 (1997)); Kakizawa, T., et al. (J. Biol. Chem. 272(38):23799-23804 (1997)); and Chang, K. H., et al. (Proc. Natl. Acad. Sci. USA 94(17):9040-9045 (1997)), which references are incorporated herein in their entirety by reference.

#### NUCLEAR RECEPTOR ISOFORMS

The present invention also is applicable to generating new synthetic ligands to distinguish nuclear receptor isoforms. As described herein, CDLs can be generated that distinguish between binding isoforms, thereby allowing the generation of either tissue specific or function specific synthetic ligands. For instance, GR subfamily members have usually one receptor encoded by a single gene, although are exceptions. For example, there are two PR isoforms, A and B, translated from the same mRNA by alternate initiation from different AUG codons. There are two GR forms, one of which does not bind ligand. This method is especially applicable to the TR subfamily which usually has several receptors that are encoded by at least two (TR: α, β) or three (RAR, RXR, and PPAR: α, β, γ) genes or have alternate RNA splicing and such an example for TR is described herein.

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#### **NUCLEAR RECEPTOR CRYSTALS**

The invention provides for crystals made from nuclear receptor ligand binding domains with the ligand bound to the receptor. As exemplified in the Examples, TRs are crystallized with a ligand bound to it. Crystals are made from purified nuclear receptor LBDs that are usually expressed by a cell culture, such as *E. coli*. Preferably, different crystals (co-crystals) for the same nuclear receptor are separately made using different ligands, such as a naturally occurring ligand and at least one bromo- or iodosubstituted synthetic ligand that acts as an analog or antagonist of the naturally occurring ligand. Such bromo- and iodo- substitutions act as heavy atom substitutions in nuclear receptor ligands and crystals of nuclear receptor proteins. This method has the advantage for phasing of the crystal in that it bypasses the need for obtaining traditional heavy metal derivatives. After the three dimensional structure is determined for the nuclear receptor LBD with its ligand bound, the three dimensional

structure can be used in computational methods to design a synthetic ligand for the nuclear receptor and further activity structure relationships can be determined through routine testing using the assays described herein and known in the art.

### 5 Expression and Purification of other Nuclear Receptor LBD Structures

High level expression of nuclear receptor LBDs can be obtained by the techniques described herein as well as others described in the literature. High level expression in E. coli of ligand binding domains of TR and other nuclear receptors, including members of the steroid/thyroid receptor superfamily, such as the receptors 10 ER, AR, MR, PR, RAR, RXR and VDR can also be achieved. Yeast and other eukaryotic expression systems can be used with nuclear receptors that bind heat shock proteins as these nuclear receptors are generally more difficult to express in bacteria, with the exception of ER, which can be expressed in bacteria. Representative nuclear receptors or their ligand binding domains have been cloned and sequenced: human 15 RAR-α, human RAR-γ, human RXR-α, human RXR-β, human PPAR-α, human PPAR-β, human PPAR-γ, human VDR, human ER (as described in Seielstad et al., Molecular Endocrinology, vol 9:647-658 (1995), incorporated herein by reference), human GR, human PR, human MR, and human AR. The ligand binding domain of each of these nuclear receptors has been identified and is shown in FIG. 3. Using the 20 information in FIG. 3 in conjunction with the methods described herein and known in the art, one of ordinary skill in the art could express and purify LBDs of any of the nuclear receptors, including those illustrated in FIG. 3, bind it to an appropriate ligand, and crystallize the nuclear receptor's LBD with a bound ligand.

FIG. 3 is an alignment of several members of the steroid/thyroid hormone 25 receptor superfamily that indicates the amino acids to be included in a suitable expression vector.

Extracts of expressing cells are a suitable source of receptor for purification and preparation of crystals of the chosen receptor. To obtain such expression, a vector is constructed in a manner similar to that employed for expression of the rat TR 30 alpha (Apriletti *et al. Protein Expression and Purification, 6*:363-370 (1995), herein incorporated by reference). The nucleotides encoding the amino acids encompassing the ligand binding domain of the receptor to be expressed, for example the estrogen receptor ligand binding domain (hER-LBD) (corresponding to R at position 725 to L

at position 1025 as standardly aligned as shown in the **FIG. 3**), are inserted into an expression vector such as the one employed by Apriletti et al (1995). For the purposes of obtaining material that will yield good crystals it is preferable to include at least the amino acids corresponding to human TR-β positions 725 to 1025. Stretches of adjacent amino acid sequences may be included if more structural information is desired. Thus, an expression vector for the human estrogen receptor can be made by inserting nucleotides encoding amino acids from position 700 to the c-terminus at position 1071. Such a vector gives high yield of receptor in E. coli that can bind hormone (Seielstad *et al. Molecular Endocrinology 9*:647-658 (1995)). However, the c-terminal region beyond position 1025 is subject to variable proteolysis and can advantageously be excluded from the construct, this technique of avoiding variable proteolysis can also be applied to other nuclear receptors.

# TR-α And TR-β As Examples of Nuclear receptor LBD Structure and Function 15 TR Expression, Purification And Crystallization

As an example of nuclear receptor structure of the ligand binding domain the α- and β- isoforms of TR are crystallized from proteins expressed from expression constructs, preferably constructs that can be expressed in E. coli. Other expression systems, such as yeast or other eukaryotic expression systems can be used. For the 20 TR, the LBD can be expressed without any portion of the DBD or amino-terminal domain. Portions of the DBD or amino-terminus can be included if further structural information with amino acids adjacent the LBD is desired. Generally, for the TR the LBD used for crystals will be less than 300 amino acids in length. Preferably, the TR LBD will be at least 150 amino acids in length, more preferably at least 200 amino acids in length, and most preferably at least 250 amino acids in length. For example the LBD used for crystallization can comprise amino acids spanning from Met 122 to Val 410 of the rat TR-α, Glu 202 to Asp 461 of the human TR-β.

Typically TR LBDs are purified to homogeneity for crystallization. Purity of TR LBDs is measured with sodium dodecyl sulfate polyacrylamide gel 30 electrophoresis (SDS-PAGE), mass spectrometry (MS) and hydrophobic high performance liquid chromatography (HPLC). The purified TR for crystallization should be at least 97.5 % pure or 97.5%, preferably at least 99.0% pure or 99.0% pure, more preferably at least 99.5% pure or 99.5% pure.

Initially purification of the unliganded receptor can be obtained by conventional techniques, such as hydrophobic interaction chromatography (HPLC), ion exchange chromatography (HPLC), and heparin affinity chromatography.

To achieve higher purification for improved crystals of nuclear receptors, 5 especially the TR subfamily and TR, it will be desirable to ligand shift purify the nuclear receptor using a column that separates the receptor according to charge, such as an ion exchange or hydrophobic interaction column, and then bind the eluted receptor with a ligand, especially an agonist. The ligand induces a change in the receptor's surface charge such that when re-chromatographed on the same column, 10 the receptor then elutes at the position of the liganded receptor are removed by the original column run with the unliganded receptor. Usually saturating concentrations of ligand are used in the column and the protein can be preincubated with the ligand prior to passing it over the column. The structural studies detailed herein indicate the general applicability of this technique for obtaining super-pure nuclear receptor LBDs for crystallization.

More recently developed methods involve engineering a "tag" such as with histidine placed on the end of the protein, such as on the amino terminus, and then using a nickle chelation column for purification, Janknecht R., *Proc. Natl. Acad. Sci. USA*, 88:8972-8976 (1991) incorporated by reference.

To determine the three dimensional structure of a TR LBD, or a LBD from 20 another member of the nuclear receptor superfamily, it is desirable to co-crystalize the LBD with a corresponding LBD ligand. In the case of TR LBD, it is preferable to separately co-crystalize it with ligands such as T3, IpBr and Dimit that differ in the heavy atoms which they contain. Other TR ligands such as those encompassed by 25 Formula 1 described herein and known in the prior art, can also be used for the generation of co-crystals of TR LBD and TR ligands. Of the compounds encompassed by Formula 1 it is generally desirable to use at least one ligand that has at least one bromo- or iodo- substitution at the R<sub>3</sub>, R<sub>5</sub>, R<sub>3</sub>' or R<sub>5</sub>' position, preferably such compounds will be have at least two such substitutions and more preferably at 30 least 3 such substitutions. As described herein, such substitutions are advantageously used as heavy atoms to help solve the phase problem for the three dimensional structure of the TR LBD and can be used as a generalized method of phasing using a halogen (e.g. I or Br) substituted ligand, especially for nuclear receptors.

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Typically purified LBD, such as TR LBD, is equilibrated at a saturating concentration of ligand at a temperature that preserves the integrity of the protein. Ligand equilibration can be established between 2 and 37°C, although the receptor tends to be more stable in the 2-20°C range.

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Preferably crystals are made with the hanging drop methods detailed herein. Regulated temperature control is desirable to improve crystal stability and quality. Temperatures between 4 and 25°C are generally used and it is often preferable to test crystallization over a range of temperatures. In the case of TR it is preferable to use crystallization temperatures from 18 to 25°C, more preferably 20 to 23°C, and most 10 preferably 22°C.

Complexes of the TR- $\alpha$  LBD with a variety of agonists, including T<sub>3</sub>, IpBr<sub>2</sub>, Dimit, and Triac, are prepared with by methods described herein. For example, cocrystals of the rTR-α LBD, with ligand prebound, are prepared by vapor diffusion at ambient temperature from 15% 2-methyl-2,4-pentanediol (MPD). The crystals are 15 radiation sensitive, and require freezing to measure complete diffraction data. On a rotating anode X-ray source, the crystals diffract to ~3Å; synchrotron radiation extends the resolution limit significantly, to as high as 2.0Å for T<sub>3</sub> cocrystals. The composition of the thyroid hormone, combined with the ability to prepare and cocrystallize the receptor complexed with a variety of analogs, permitted the unusual 20 phasing strategy. This phasing strategy can be applied to the ligands of the nuclear receptors described therein by generating I and Br substitutions of such ligands. In this strategy, cocrystals of the TR LBD containing four hormone analogs that differ at the 3,5, and 3' positions (T3, IpBr2, Dimit, and Triac) provided isomorphous derivatives. For this set of analogs, the halogen substituents (2Br and 3I atoms) 25 function as heavy atoms, while the Dimit cocrystal (3 alkyl groups) acts as the parent. The initial 2.5Å multiple isomorphous replacement/anomalous scattering/density modified electron density map allowed the LBD to be traced from skeletons created in the molecular graphics program O5 (Jones, T.A. et al., ACTA Cryst, 47:110-119 (1991), incorporated by reference herein). A model of the LBD was built in four 30 fragments, Arg157-Gly184, Trp186-Gly197, Ser199-Pro205, and Val210-Phe405, and refined in XPLOR using positional refinement and simulated annealing protocols. Missing residues were built with the aid of difference density. The final model was refined to  $R_{cryst} = 21.8\%$  and  $R_{free} = 24.4\%$  for data from 15.0 to 2.2Å, see **Table 6**.

The human TR- $\beta$  LBD model was resolved by molecular replacement of the TR- $\alpha$  LBD coordinates. The structure is based on E202 to D461 with a his-tag at the N-terminus. The final model was refined to R<sub>cryst</sub> = 25.3% and R<sub>free</sub> = 28.9% for data from 30.0 to 2.4Å+, see Table 7.

This phasing strategy can be applied to the ligands of the nuclear receptors described herein by generating I and Br substitutions of such ligands.

# THREE DIMENSIONAL STRUCTURE OF TR LBD Architecture of TR LBD

As an example of the three dimensional structure of a nuclear receptor, the folding of the TR-α LBD is shown in **FIG. 4**. The TR-α LBD consists of a single structural domain packed in three layers, composed of twelve α-helices, H1-12, and four short β-strands, S1-4, forming a mixed β-sheet. The buried hormone and three antiparallel α-helices, H5-6, H9, and H10, form the central layer of the domain, as shown in **FIG. 4**. H1, H2, H3 and S1 form one face of the LBD, with the opposite face formed by H7, H8, H11, and H12. The first 35 amino acids of the N-terminus (Met122-Gln156) are not visible in the electron density maps. The three dimensional structure of the heterodimeric RXR:TR DNA-binding domains bound to DNA, amino acids Met 122 - Gln151 of the TR DBD make extensive contacts with the minor 20 groove of the DNA8. The five disordered amino acids (Arg152-Gln156), which reside between the last visible residue of the TR DBD and the first visible residue of the LBD likely represent the effective "hinge" linking the LBD and the DBD in the intact receptor.

The predominantly helical composition and the layered arrangement of 25 secondary structure is identical to that of the unliganded hRXRα, confirming the existence of a common nuclear receptor fold between two nuclear receptors.

The TR LBD is visible beginning at Arg157, and continues in an extended coil conformation to the start of H1. A turn of α-helix, H2, covers the hormone binding cavity, immediately followed by short β-strand, S1, which forms the edge of the 30 mixed β-sheet, parallel to S4, the outermost of the three antiparallel strands. The chain is mostly irregular until H3 begins, antiparallel to H1. H3 bends at Ile221 and IIe222, residues which contact the ligand. The chain turns almost 90° at the end of H3 to form an incomplete α-helix, H4. The first buried core helix, H5-6, follows, its axis

altered by a kink near the ligand at Gly 253. The helix is composed of mostly hydrophobic sidechains interrupted by two striking exceptions: Arg262 is solvent inaccessible and interacts with the ligand carboxylate (1-substituent), and Glu256 meets Arg329 from H9 and Arg375 from H11 in a polar invagination. 5 terminates in a short β-strand, S2, of the four strand mixed sheet. S3 and S4 are joined through a left-handed turn, and further linked by a salt bridge between Lys284 and Asp272. Following S4, H7 and H8 form an L, stabilized by a salt bridge between Lys268 and Asp277. The turn between H7 and H8 adopts an unusual conformation, a result of interaction with ligand and its glycine rich sequence. H9 is the second core 10 helix. antiparallel to the neighboring H5-6. Again, two buried polar sidechains are found, Glu315 and Gln320. Glu315 forms a buried salt bridge with His358 and Arg356. The oxygen of Gln320 forms a hydrogen bond with the buried sidechain of His 175. The chain then switches back again to form H10, also antiparallel to H9. H11 extends diagonally across the full length of the molecule. Immediately after H11, the 15 chain forms a type II turn, at approximately 90° to H11. The chain then turns again to form H 12, which packs loosely against H3 and H11 as part of the hormone or ligand binding cavity. The final five amino acids at the C-terminus, Glu406 -Val410, are disordered. The architecture of the TR- $\beta$  LBD is identical to that of the TR- $\alpha$  LBD, with two significant differences. An additional helix is present at the N-terminus 20 (residues Glu202-I1e208), which is part of the DBD, and packs antiparallel to H10. Following the helix is a two residue turn (Gly209-His210) continuing into an extended coil to he start of H1, as seen in the TR-α LBD. A further difference occurs in the irregular conformation adopted between H2 and H3. In the TR-α LBD, residue Gly197-Asp211 form a loop that packs against the receptor, contacting helices H7, 25 H8, H11, and the loop between H11 and H12. In the TR-β LBD, only the ends of the loop are ordered, with the stretch Ala253-Lys263 disordered. In addition to these residues, the residues of the His-tag at the N-terminus, and the final residue at the Cterminus, Asp461, are disordered.

# 30 TR LBD's Ligand Binding Cavity As An Example Of A Nuclear Receptor's Buried Ligand Cavity

The three dimensional structure of the TR LBD leads to the startling finding that ligand binding cavity of the LBD is solvent inaccessible when a T3 or its isostere

is bound to the LBD. This surprising result leads to a new model of nuclear receptor three dimensional structure and function, as further described herein, particularly in the sections elucidating the computational methods of ligand design and the application of such methods to designing nuclear receptor synthetic ligands that 5 contain extended positions that prevent normal activation of the activation domain.

Dimit, the ligand bound to the receptor, is an isostere of T<sub>3</sub> and a thyroid hormone agonist. Therefore the binding of Dimit should reflect that of T<sub>3</sub>, and the Dimit-bound receptor is expected to be the active conformation of TR. The ligand is buried within the receptor, providing the hydrophobic core for a subdomain of the 10 protein, as shown in **FIG. 5 a and b**. H5-6 and H9 comprise the hydrophobic core for the rest of the receptor.

An extensive binding cavity is constructed from several structural elements. The cavity is enclosed from above by H5-6 (Met 256- Arg266), from below by H7 and H8 and the intervening loop (Leu287- Ile299), and along the sides by H2 (185- 187), by the turn between S3 and S4 (Leu276-Ser277), by H3 (Phe215-Arg228), by H11 (His381-Met388) and by H12 (Phe401-Phe405). The volume of the cavity defined by these elements, calculated by GRASP (Columbia University, USA) (600 Å3), is essentially the volume of the hormone (530 Å). The change in volume can be exploited for ligand design as described herein. The remaining volume is occupied by water molecules surrounding the amino-propionic acid substituent. **FIG. 6** depicts various contacts (or interactions) between TR's LBD and the ligand.

The planes of the inner and outer (prime ring) rings of the ligand are rotated from planarity about 60° with respect to each other, adopting the 3'-distal conformation (in which the 3' substituent of the outer ring projects down and away 25 from the inner ring). The amino-propionic acid and the outer phenolic ring assume the transoid conformation, each on opposite sides of the inner ring. The torsion angle χ<sub>1</sub> for the amino- propionic acid is 300°.

The amino-propionic acid substituent is packed loosely in a polar pocket formed by side chains from H2, H4 and S3. The carboxylate group forms direct 30 hydrogen bonds with the guanidium group of Arg228 and the amino N of Ser277. In addition, Arg262, Arg266 and Asn179 interact with the carboxylate through water-mediated hydrogen bonds. The three arginine residues create a significantly positive local electrostatic potential, which may stabilize the negative charge of the

carboxylate. No hydrogen bond is formed by the amino nitrogen. The interactions of the amino-propionic acid substituent are consistent with the fact that Triac, which lacks the amino nitrogen, has a binding affinity equal to that of T<sub>3</sub>, indicating that the amino nitrogen and longer aliphatic chain of T<sub>3</sub> do not contribute greatly to binding 5 affinity.

The biphenyl ether, in contrast, is found buried within the hydrophobic core. The inner ring packs in a hydrophobic pocket formed by H3, H5-6, and S3. Pockets for the 3- and 5-methyl substituents are not completely filled, as expected since the van der waals radius of methyl substituent for Dimit is smaller than the iodine substituent provided by the thyroid hormone T<sub>3</sub>. Such pockets are typically 25 to 100 cubic angstroms (although smaller pocket for substitutes are contemplated in the 40 to 80 cubic angstrom range) and could be filled more tightly with better fitting chemical substitutions, as described herein.

The outer ring packed tightly in a pocket formed by H3, H5-6, H7, H8, H11 and H12, and the loop between H7 and H8. The ether oxygen is found in a hydrophobic environment defined by Phe218, Leu287, Leu276, and Leu292. The absence of a hydrogen bond to the ether oxygen is consistent with its role in establishing the correct stereochemistry of the phenyl rings, as suggested by potent binding of hormone analogs with structurally similar linkages possessing reduced or negligible hydrogen bonding capability. The 3'-isopropyl substituent contacts Gly290 and 291. The presence of glycine at this position in the pocket can explain the observed relationship between activity and the size of 3'-substituents. Activity is highest for 3'-isopropyl, and decreases with added bulk. The only hydrogen bond in the hydrophobic cavity is formed between the phenolic hydroxyl and His381 Ne2.

25 The conformation of His381 is stabilized by packing contacts provided by Phe405, and Met256.

The presence of a 5' substituent larger than hydrogen affects the binding affinity for hormone. The more abundant thyroid hormone, 3,5,3',5'-tetraiodo-L-thyronine (T<sub>4</sub>), contains an iodine at this position, and binds the receptor with 2% of 30 the affinity of T<sub>3</sub>. The structure suggests that discrimination against T<sub>4</sub> is accomplished through the combination of steric conflict by Met256 and possibly the constraints imposed by the geometry of the hydrogen bond from His381 to the phenolic hydroxyl. The 5' position is a preferred location for introducing a chemical

modification of C-H at the 5' of T3 or and TR agonist, as described herein, that produces an extension from the prime ring and results in the creation of an antagonist or partial agonist.

Deletion and antibody competition studies suggest the involvement of residues

Pro162 to Val202 in ligand binding. The region does not directly contact hormone in
the bound structure, although H2 packs against residues forming the polar pocket that
interacts with the amino-propionic acid group. One role for H2, then, is to stabilize
these residues in the bound state, H2, with β-strands S3 and S4, might also represent a
prevalent entry point for ligand, since the amino-propionic acid of the ligand is
oriented toward this region. Studies of receptor binding to T3 affinity matrices
demonstrate that only a linkage to the amino-propionic acid is tolerated, suggesting
that steric hindrance present in other linkages prevent binding. Furthermore, the
crystallographic temperature factors suggest the coil and β-strand region is most
flexible part of the domain FIG. 7. Participation of this region, part of the hinge
domain between the DBD and LBD, in binding hormone may provide structural
means for ligand binding to influence DNA binding, since parts of the Hinge domain
contact DNA.

# TR LBD Transcriptional Activation Helix As An Example Of A Nuclear Receptor 20 Activation Domain

In addition to the startling finding that the ligand binding cavity is solvent inaccessible when loaded with a ligand, the activation helix of TR LBD presents a surface to the ligand cavity for interaction between at least one amino acid and the bound ligand. The C-terminal 17 amino acids of the TR, referred to as the activation 25 helix or AF-2 (an example of an LBD activation domain), are implicated in mediating hormone-dependent transcriptional activation. Although, mutations of key residues within the domain decrease ligand-dependent activation it was unclear until the present invention whether such mutations directly affected ligand coordination. Although some mutations of this domain have been noted to reduce or abolish ligand 30 binding, other mutations in more distant sites of the LBD have a similar effect.

Activation domains among nuclear receptors display an analogous three dimensional relationship to the binding cavity, which is a region of the LBD that binds the molecular recognition domain of a ligand, i.e. the activation domain

presents a portion of itself to the binding cavity (but necessarily the molecular recognition domain of the ligand). Many nuclear receptors are expected to have such domains, including the retinoid receptors, RAR and RXR, the glucocorticoid receptor GR, and the estrogen receptor ER. Based upon the TR's sequence, the domain is proposed to adopt an amphipathic helical structure. β-sheet or mixed secondary structures, could be present as activation domains in less related nuclear receptors.

Within the activation domain, the highly conserved motif ΦΦΧΕΦΦ, where Φ represents a hydrophobic residue, is proposed to mediate interactions between the receptors and transcriptional coactivators. Several proteins have been identified 10 which bind the TR in a hormone-dependent fashion. One of these, Trip1, is related to a putative yeast coactivator Sug1, and also interacts with both the C-terminal activation domain and a subset of the basal transcriptional machinery, suggesting a role in transactivation by the TR. Other proteins, such as RIP140, SRC1, (Onate, S.A. et. al., *Science* 270:1354-1357 (1995)) and TF-1 (see also Ledouarim, B., et. al., 15 *EMBO J.* 14:2020-2033 (1995)), and GRIP-1 (Heery, E., et al., Nature 387:733-736 (1997)) also interact with other nuclear receptors in a ligand dependent manner through the C-terminal domain. Binding of these proteins can be modulated using the TR ligands described herein especially those TR ligands with extensions that sterically hinder the interaction between the highly conserved motif and other 20 proteins.

The C-terminal activation domain of the TR forms an amphipathic helix, H12, which nestles loosely against the receptor to form part of the hormone binding cavity. The helix packs with the hydrophobic residues facing inward towards the hormone binding cavity, and the charged residues, including the highly-conserved glutamate, extending into the solvent, as shown in FIG. 8. The activation helix of TR LBD presents Phe 401 to the ligand binding cavity and permits direct coordination with the hormone i.e. such amino acids interact with the ligand forming a van der waals contact with the plane of the outer phenyl ring. Phe 405 also interacts with His 381, perhaps stabilizing its hydrogen bonding conformation, i.e. a favorable hydrogen bond interaction. Participation of Phe 401 and Phe 405 in binding hormone explains how mutation of these residues decreases hormone binding affinity. Furthermore, the impact of these mutations on activation likely derives from a role in stabilizing the domain in the bound structure through increased hydrogen bond interaction of dipole

interactions. Glu 403 extends into the solvent, emphasizing its critical role in transactivation. In its observed conformation, presented on the surface as an ordered residue, against a background of predominantly hydrophobic surface, Glu 403 is available to interact with activator proteins described herein, as shown in **FIG. 9**. The other charged residues, Glu 405 and Asp 406 are disordered, as the helix frays at Phe 405.

Two other sequences in the TR, τ2 and τ3, activate transcription when expressed as fusion proteins with a DNA-binding domain. The sequences, discovered in the TRB, correspond to TR-α residues Pro158-Ile168 in H1 (τ2), and Gly290-Leu3 10 19 in H8 and H9 (τ3). Unlike the C-terminal activation domain, τ2 and τ3 do not appear to represent modular structural units in the rat TR-I LBD, nor present a surface for protein-protein interactions: the critical aspartate/glutamate residues of τ3 are located on two separate helices, and do not form a single surface; the charged residues of τ2 are engaged in ion pair interactions with residues of the LBD. Thus, τ2 and τ3 may not function as activation domains in the context of the entire receptor.

# Computational Methods For Designing A Nuclear Receptor LBD LIGAND

The elucidation of the three dimensional structure of a nuclear receptor ligand binding domain provides an important and useful approach for designing ligands to nuclear receptors using the computational methods described herein. By inspecting the **FIGURES** it can be determined that the nuclear receptor ligand is bound in a water inaccessible binding cavity in the LBD and that chemical moieties can be added to selected positions on the ligand. Such chemical modifications, usually extensions, can fill up the binding cavity represented in the **FIGURES** for a tighter fit (or less water) or can be used to disrupt or make contacts with amino acids not in contact with the ligand before the chemical modification was introduced or represented in a figure of the three dimensional model of the LBD. Ligands that interact with nuclear superfamily members can act as agonists, antagonists and partial agonists based on what ligand-induced conformational changes take place.

Agonists induce changes in receptors that place them in an active conformation that allows them to influence transcription, either positively or negatively. There may be several different ligand-induced changes in the receptor's conformation.

Antagonists, bind to receptors, but fail to induce conformational changes that alter the receptor's transcriptional regulatory properties or physiologically relevant conformations. Binding of an antagonist can also block the binding and therefore the actions of an agonist.

Partial agonists bind to receptors and induce only part of the changes in the receptors that are induced by agonists. The differences can be qualitative or quantitative. Thus, a partial agonist may induce some of the conformation changes induced by agonists, but not others, or it may only induce certain changes to a limited extent.

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# Ligand-induced Conformational Changes

As described herein, the unliganded receptor is in a configuration that is either inactive, has some activity or has repressor activity. Binding of agonist ligands induces conformational changes in the receptor such that the receptor becomes more active, either to stimulate or repress the expression of genes. The receptors may also have non-genomic actions. Some of the known types of changes and/or the sequelae of these are listed herein.

#### Heat Shock Protein Binding

For many of the nuclear receptors ligand binding induces a dissociation of heat shock proteins such that the receptors can form dimers in most cases, after which the receptors bind to DNA and regulate transcription.

Nuclear receptors usually have heat shock protein binding domains that present a region for binding to the LBD and can be modulated by the binding of a 25 ligand to the LBD. Consequently, an extended chemical moiety (or more) from the ligand that stabilizes the binding or contact of the heat shock protein binding domain with the LBD can be designed using the computational methods described herein to produce a partial agonist or antagonist. Typically such extended chemical moieties will extend past and away from the molecular recognition domain on the ligand and 30 usually past the buried binding cavity of the ligand.

#### Dimerization and Heterodimerization

With the receptors that are associated with the hsp in the absence of the ligand, dissociation of the hsp results in dimerization of the receptors. Dimerization is due to

receptor domains in both the DBD and the LBD. Although the main stimulus for dimerization is dissociation of the hsp, the ligand-induced conformational changes in the receptors may have an additional facilitative influence. With the receptors that are not associated with hsp in the absence of the ligand, particularly with the TR, ligand 5 binding can affect the pattern of dimerization/heterodimerization. The influence depends on the DNA binding site context, and may also depend on the promoter context with respect to other proteins that may interact with the receptors. A common pattern is to discourage monomer formation, with a resulting preference for heterodimer formation over dimer formation on DNA.

Nuclear receptor LBDs usually have dimerization domains that present a region for binding to another nuclear receptor and can be modulated by the binding of a ligand to the LBD. Consequently, an extended chemical moiety (or more) from the ligand that disrupts the binding or contact of the dimerization domain can be designed using the computational methods described herein to produce a partial agonist or antagonist. Typically such extended chemical moieties will extend past and away from the molecular recognition domain on the ligand and usually past the buried binding cavity of the ligand.

#### DNA Binding

20 In nuclear receptors that bind to hsp, the ligand-induced dissociation of hsp with consequent dimer formation allows, and therefore, promotes DNA binding. With receptors that are not associated (as in the absence of ligand), ligand binding tends to stimulate DNA binding of heterodimers and dimers, and to discourage monomer binding to DNA. However, ligand binding to TR, for example, tends to 25 decrease dimer binding on certain DNA elements and has minimal to no effect on increasing heterodimer binding. With DNA containing only a single half site, the ligand tends to stimulate the receptor's binding to DNA. The effects are modest and depend on the nature of the DNA site and probably on the presence of other proteins that may interact with the receptors. Nuclear receptors usually have DBDs that 30 present a region for binding to DNA and this binding can be modulated by the binding of a ligand to the LBD. Consequently, an extended chemical moiety (or more) from the ligand that disrupts the binding or contact of the DBD can be designed using the computational methods described herein to produce a partial agonist or antagonist. Typically such extended chemical moieties will extend past and away from the

molecular recognition domain on the ligand and usually past the buried binding cavity of the ligand.

#### Repressor Binding

Receptors that are not associated with hsp in the absence of ligand frequently act as transcriptional repressors in the absence of the ligand. This appears to be due, in part, to transcriptional repressor proteins that bind to the LBD of the receptors. Agonist binding induces a dissociation of these proteins from the receptors. This relieves the inhibition of transcription and allows the transcriptional transactivation 10 functions of the receptors to become manifest.

#### Transcriptional Transactivation Functions

Ligand binding induces transcriptional activation functions in two basic ways. The first is through dissociation of the hsp from receptors. This dissociation, with consequent dimerization of the receptors and their binding to DNA or other proteins in the nuclear chromatin allows transcriptional regulatory properties of the receptors to be manifest. This may be especially true of such functions on the amino terminus of the receptors.

The second way is to alter the receptor to interact with other proteins involved 20 in transcription. These could be proteins that interact directly or indirectly with elements of the proximal promoter or proteins of the proximal promoter. Alternatively, the interactions could be through other transcription factors that themselves interact directly or indirectly with proteins of the proximal promoter. Several different proteins have been described that bind to the receptors in a ligand-25 dependent manner. In addition, it is possible that in some cases, the ligand-induced conformational changes do not affect the binding of other proteins to the receptor, but do affect their abilities to regulate transcription.

Nuclear receptors or nuclear receptor LBDs usually have activation domains modulated in part by a co-activator/co-repressor system that coordinately functions to 30 present a region for binding to DNA, and can be modulated by the binding of a ligand to the LBD. Consequently, an extended chemical moiety (or more) from the ligand that disrupts the binding or contact of the activation domain with co-activator and/or co-repressor can be designed using the computational methods described herein to produce a partial agonist or antagonist. For instance, an agonist can be designed

and/or selected which (1) blocks binding and/or dissociates co-repressor, and/or (2) promotes binding and/or association of a co-activator. An antagonist can be designed which (1) promotes binding and/or association of co-repressor, and/or (2) promotes binding and/or association of co-activator. Ratios of agonists and antagonists may be 5 used to modulate transcription of the gene of interest. Selection can be accomplised in binding assays that screen for ligands having the desired agonist or antagonist properties, including such ligands which induce conformational changes as decribed below. Suitable assays for such screening are described herein and in Shibata, H., et al. (Recent Prog. Horm. Res. 52:141-164 (1997)); Tagami, T., et al. (Mol. Cell Biol. 10 17(5):2642-2648 (1997)); Zhu, XG., et al. (J. Biol. Chem. 272(14):9048-9054 (1997)); Lin, B.C., et al. (Mol. Cell Biol. 17(10):6131-6138 (1997)); Kakizawa, T., et al. (J. Biol. Chem. 272(38):23799-23804 (1997)); and Chang, K. H., et al. (Proc. Natl. Acad. Sci. USA 94(17):9040-9045 (1997)). Typically such extended chemical moieties will extend past and away from the molecular recognition domain on the 15 ligand and usually past the buried binding cavity of the ligand and in the direction of the activation domain, which is often a helix as seen in the three dimensional model shown in the FIGURES in two dimensions on paper or more conveniently on a computer screen.

#### 20 Ligand-Induced Conformational Change

Plasma proteins bind hormones without undergoing a conformational change through a static binding pocket formed between monomers or domains. For example, the tetrameric thyroid-binding plasma protein transthyretin forms a solvent-accessible hormone-binding channel at the oligomer interface. The structure of the protein is unchanged upon binding hormone with respect to the appearance of a buried binding cavity with a ligand bound.

However, the structural role for a ligand bound to a nuclear receptor LBD, like rat TR-α LBD, predicts that the receptor would differ in the bound and unbound states. In the absence of hormone, the receptor would possess a cavity at its core, 30 uncharacteristic of a globular protein. A ligand (e.g. hormone) completes the hydrophobic core of the active receptor after it binds to the nuclear receptor. Ligand binding by the receptor is a dynamic process, which regulates receptor function by inducing an altered conformation.

An exact description of the hormone-induced conformational changes requires comparison of the structures of the liganded and the unliganded TR. The structure of the unliganded human RXRα may substitute as a model for the unliganded TR. The rat TR-α LBD and human RXRα LBDs adopt a similar fold, and it is likely that the 5 structural similarity extends to the conformational changes after ligand binding.

There are three major differences between the two structures, which indeed appear to be the result of ligand binding. First, the bound rat TR-α LBD structure is more compact, with the hormone tightly packed within the hydrophobic core of the receptor. By contrast, the unliganded human RXRα LBD contains several internal 10 hydrophobic cavities. The presence of such cavities is unusual in folded proteins, and is likely a reflection of the unliganded state of the receptor. Two of these cavities were proposed as possible binding sites for 9-cis retinoic acid, though these multiple sites only partly overlap with the single buried binding cavity observed in the liganded rat TR-α LBD.

15 The second difference involves H11 in the rat TR-α LBD, which contributes part of the hormone binding cavity. H11, continuous in the rat TR-α LBD, is broken at Cys 432 in the RXR, forming a loop between H10 and H11 in the hRXRα. This residue corresponds to His381 in the TR, which provides a hydrogen bond to the outer ring hydroxyl of the ligand. Furthermore, the hormone binding cavity occupied by 20 ligand in the rat TR-α LBD is interrupted in the hRXRα by the same loop, forming an isolated hydrophobic pocket in the RXR with H6 and H7. In the bound rat TR-α LBD, the corresponding helices H7 and H8 are contiguous with the binding pocket, and enclose the hormone binding cavity from below.

The third difference between the two receptors is the position of the C-25 terminal activation domain. While the C-terminal activation domain forms α-helices in both receptors, the domain in the rat TR-α LBD follows a proline-rich turn, and lies against the receptor to contribute part of the binding cavity. In contrast, the activation domain in the unliganded hRXRα, is part of a longer helix which projects into the solvent.

These differences lead to a model for an alternate conformation of the TR LBD assumed in the absence of ligand. In the unliganded TR, the subdomain of the receptor surrounding the hormone binding cavity is loosely packed, with the binding cavity occluded by a partly unstructured H11 providing a partial core for the receptor.

Upon binding hormone, residues which form a coil in the unbound receptor engage the ligand, and continues H11. The ordering of H11 could unblock the hydrophobic cavity, allowing H7 and H8 to interact with hormone. The extended hydrophobic cavity then collapses around the hormone, generating the compact bound 5 structure.

It is possible to predict ligand-induced conformational changes in the C-terminal activation domain that rely, in part, on an extended structure in the unliganded TR that repacks upon ligand binding. The ligand- induced conformation change can be subtle since the amino acid sequence of the rat TR-α in the turn (393-10 PTELFPP-399) significantly reduces the propensity of the peptide chain of the rat TR-α to form an α-helix and therefore repacking can be accomplished with a minor change in volume.

After the ligand-induced conformational change occurs, it is likely that the conformation of the C-terminal activation domain in the bound structure changes 15 packing compared to the unbound form of the receptor. Binding of the ligand improves the stability of the activation domain. The activation domain packs loosely even in the bound structure, as measured by the distribution of packing interactions for the entire LBD. The packing density for the activation domain, defined as the number of atoms within 4.5Å, is 1.5 standard deviations below the mean. For 20 comparison, another surface helix, H1, is 0.5 standard deviations below the mean and the most poorly packed part of the structure, the irregular coil from residues Ile196-Asp206, is 2.0 standard deviations below the mean. Moreover, the majority of packing contacts for the C-terminal domain in the bound receptor are provided either by residues which interact with ligand, such as His381, or by the ligand itself. The 25 conformation of these residues can be expected to be different in the bound and unbound receptors, and by extension the conformation of C-terminal activation domain which relies upon these interactions. Without the stabilization provided by a bound ligand, it is likely that the C-terminal activation domain is disordered prior to hormone binding.

The interrelation of ligand-induced conformational changes is evident as described herein. For example, His381 from H11 and Phe405 from H12 interact in the bound structure to provide a specific hydrogen bond to the phenolic hydroxyl. The

ligand-induced changes which affect H11 and H12 are reinforcing, and lead to the formation of the compact, bound state.

Comparison of the TR- $\alpha$  and TR- $\beta$  LBD structures shows similar packing of the helices when complexed with the ligand Triac.

# COMPUTATIONAL METHODS USING THREE DIMENSIONAL MODELS AND EXTENSIONS OF LIGANDS

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The three-dimensional structure of the liganded TR receptor is unprecedented, and will greatly aid in the development of new nuclear receptor synthetic ligands, 10 such as thyroid receptor antagonists and improved agonists, especially those that bind selectively to one of the two TR isoforms ( $\alpha$  or  $\beta$ ). In addition, this receptor superfamily is overall well suited to modern methods including three-dimensional structure elucidation and combinatorial chemistry such as those disclosed in EP 335 628, U.S. patent 5,463,564, which are incorporated herein by reference. Structure 15 determination using X-ray crystallography is possible because of the solubility properties of the receptors. Computer programs that use crystallography data when practicing the present invention will enable the rational design of ligand to these receptors. Programs such as RASMOL can be used with the atomic coordinates from crystals generated by practicing the invention or used to practice the invention by 20 generating three dimensional models and/or determining the structures involved in ligand binding. Computer programs such as INSIGHT and GRASP allow for further manipulation and the ability to introduce new structures. In addition, high throughput binding and bioactivity assays can be devised using purified recombinant protein and modern reporter gene transcription assays described herein and known in the art in 25 order to refine the activity of a CDL.

Generally the computational method of designing a nuclear receptor synthetic ligand comprises two steps:

- determining which amino acid or amino acids of a nuclear receptor LBD interacts with a first chemical moiety (at least one) of the ligand using a three
   dimensional model of a crystallized protein comprising a nuclear receptor LBD with a bound ligand, and
  - 2) selecting a chemical modification (at least one) of the first chemical moiety to produce a second chemical moiety with a structure to either decrease or increase an

interaction between the interacting amino acid and the second chemical moiety compared to the interaction between the interacting amino acid and the first chemical moiety.

As shown herein, interacting amino acids form contacts with the ligand and 5 the center of the atoms of the interacting amino acids are usually 2 to 4 angstroms away from the center of the atoms of the ligand. Generally these distances are determined by computer as discussed herein and in McRee 1993, however distances can be determined manually once the three dimensional model is made. Examples of interacting amino acids are described in Appendix 2. See also Wagner et al., Nature 10 378(6558):670-697 (1995) for stereochemical figures of three dimensional models. More commonly, the atoms of the ligand and the atoms of interacting amino acids are 3 to 4 angstroms apart. The invention can be practiced by repeating steps 1 and 2 to refine the fit of the ligand to the LBD and to determine a better ligand, such as an agonist. As shown in the FIGURES the three dimensional model of TR can be 15 represented in two dimensions to determine which amino acids contact the ligand and to select a position on the ligand for chemical modification and changing the interaction with a particular amino acid compared to that before chemical modification. Structural comparison of LBD isoforms complexed with the same or similar ligand permit identification of fiducial and adjustable amino acids that can be 20 exploited in designing isoform-specific ligands through chemical modification. "Fiducial" refers to amino acids that form rigid features of the ligand binding cavity. "Adjustable" refers to amino acids that form less rigid features of the ligand binding cavity. The chemical modification may be made using a computer, manually using a two dimensional representation of the three dimensional model or by chemically 25 synthesizing the ligand. The three dimensional model may be made using Appendix 2 and the FIGURES. As an additional step, the three dimensional model may be made using atomic coordinates of nuclear receptor LBDs from crystallized protein as known in the art, see McRee 1993 referenced herein.

The ligand can also interact with distant amino acids after chemical modification of the ligand to create a new ligand. Distant amino acids are generally not in contact with the ligand before chemical modification. A chemical modification can change the structure of the ligand to make as new ligand that interacts with a distant amino acid usually at least 4.5 angstroms away from the ligand. Often distant

amino acids will not line the surface of the binding cavity for the ligand, as they are too far away from the ligand to be part of a pocket or surface of the binding cavity.

The interaction between an atom of a LBD amino acid and an atom of an LBD ligand can be made by any force or attraction described in nature. Usually the 5 interaction between the atom of the amino acid and the ligand will be the result of a hydrogen bonding interaction, charge interaction, hydrophobic interaction, van der waals interaction or dipole interaction. In the case of the hydrophobic interaction it is recognized that this is not a per se interaction between the amino acid and ligand, but rather the usual result, in part, of the repulsion of water or other hydrophilic group 10 from a hydrophobic surface. Reduction or enhancment of the interaction of the LBD and a ligand can be measured by standard binding procedures, calculating or testing binding energies, computationally or using thermodynamic or kinetic methods as known in the art.

Chemical modifications will often enhance or reduce interactions of an atom 15 of a LBD amino acid and an atom of an LBD ligand. Steric hinderance will be a common means of changing the interaction of the LBD binding cavity with the activation domain. Chemical modifications are preferably introduced at C-H, C- and C-OH position in ligands, where the carbon is part of the ligand structure which remains the same after modification is complete. In the case of C-H, C could have 1, 2 or 3 hydrogens, but usually only one hydrogen will be replaced. The H or OH are removed after modification is complete and replaced with the desired chemical moiety.

Because the thyroid receptor is a member of the larger superfamily of hormone-binding nuclear receptors, the rules for agonist and antagonist development will be recognized by one skilled in the art as useful in designing ligands to the entire superfamily. Examining the structures of known agonists and antagonists of the estrogen and androgen receptors supports the generality of antagonist mechanism of action as shown in **FIG. 10**.

The overall folding of the receptor based on a comparison of the reported structure of the unliganded RXR and with amino acid sequences of other superfamily members reveals that the overall folding of receptors of the superfamily is similar. Thus, it is predicted from the structure that there is a general pattern of folding of the nuclear receptor around the agonist or antagonist ligand.

The three dimensional structure of a nuclear receptor with a ligand bound leads to the nonobvious observation that a nuclear receptor folds around agonist ligands, as the binding cavity fits the agonist, especially the agonist's molecular recognition domain, and antagonists commonly have chemical structures that extend 5 beyond the ligand, especially the agonist, and would prohibit folding of the receptor around the ligand to form a buried binding cavity or other groups that have the same effect. The location of the extension could affect the folding in various ways as indicated by the structure. Such extensions on antagonists are shown in **FIG. 10** for various receptors and compared to the corresponding agonist.

10 For example, an extension towards the carboxy-terminal activation helix affects the packing/folding of this helix into the body of the receptor. This in turn can affect the ability of this portion of the nuclear receptor to interact with other proteins or other portions of the receptor, including transcriptional transactivation functions on the opposite end of the linear receptor, or the receptor's amino terminus that may 15 interact directly or indirectly with the carboxy-terminal transactivation domain (including helix 12). Extensions in this direction can also affect the packing of helix 11 of TR (or its analogous helix in nuclear receptors) into the body of the receptor and selectively affect dimerization and heterodimerization of receptors. An extension pointing towards helix 1 can affect the relationship of the DNA binding domain and 20 hinge regions of the receptors with the ligand binding domain and selectively or in addition affect the receptors' binding to DNA and/or interactions of receptors with proteins that interact with this region of the receptor. Other extensions towards helix 11 can be made to affect the packing of this helix and helices 1 and 10 and thereby homo- and hetero-dimerization. Such chemical modifications can be assessed using 25 the computational methods described herein. It is also possible that, in some cases, extensions may protrude through the receptor that is otherwise completely or incompletely folded around the ligand. Such protruding extensions could present a steric blockade to interactions with co-activators or other proteins.

The three dimensional structure with the ligand buried in the binding cavity immediately offers a simple description of a nuclear receptor that has a binding cavity that contains hinges and a lid, composed of one or more structural elements, that move to accommodate and surround the ligand. The ligand to TR can be modified on specific sites with specific classes of chemical groups that will serve to leave the lid and hinge region in open, partially open or closed states to achieve partial agonist or

antagonist functions. In these states, the biological response of the TR is different and so the structure can be used to design particular compounds with desired effects.

Knowledge of the three-dimensional structure of the TR-T<sub>3</sub> complex leads to a general model for agonist and antagonist design. An important novel feature of the structural data is the fact that the T<sub>3</sub> ligand is completely buried within the central hydrophobic core of the protein. Other ligand-receptor complexes belonging to the nuclear receptor superfamily will have a similarly buried ligand binding site and therefore this model will be useful for agonist/antagonist design for the entire superfamily.

When design of an antagonist is desired, one needs either to preserve the important binding contacts of natural hormone agonist while incorporating an "extension group" that interferes with the normal operation of the ligand-receptor complex or to generate the requisite binding affinity through the interactions of the extensions with receptor domains.

The model applied to antagonist design and described herein is called the 15 "Extension Model." Antagonist compounds for nuclear receptors should contain the same or similar groups that facilitate high-affinity binding to the receptor, and in addition, such compounds should contain a side chain which may be large and/or polar. This side chain could be an actual extension, giving it bulk, or it could be a 20 side group with a charge function that differs from the agonist ligand. For example, substitution of a CH<sub>3</sub> for CH<sub>2</sub>OH at the 21-position, and alteration at the 11-position from an OH group to a keto group of cortisol generates glucocorticoid antagonist activity (Robsseau, G.G., et. al., J. Mol. Biol. 67:99-115 (1972)). However, in most cases effective antagonists have more bulky extensions. Thus, the antiglucocorticoid 25 (and antiprogestin) RU486 contains a bulky side group at the 11-position (Horwitz, K.B. Endocrine Rev. 13:146-163 (1992)). The antagonist compound will then bind within the buried ligand binding site of the receptor with reasonably high affinity (100 nM), but the extension function will prevent the receptor-ligand complex from adopting the necessary conformation needed for transcription factor function. The 30 antagonism (which could be in an agonist or antagonist) may manifest itself at the molecular level in a number of ways, including by preventing receptor homo/heterodimer formation at the HRE, by preventing coactivator binding to receptor monomers, homodimers or homo/heterodimers, or by a combination of these effects which otherwise prevent transcription of hormone responsive genes mediated

by ligand-induced effects on the HRE. There are several antagonist compounds for nuclear receptors in the prior art (see also Horwitz, K.B., Endocrine Rev. 13:146-163 (1992), Raunnaud J.P. et. al., J. Steroid Biochem. 25:811-833 (1986), Keiel S., et. al., Mol. Cell. Biol. 14:287-298 (1994) whose antagonist function can be explained by the extension hypothesis. These compounds are shown in FIG. 10 along with their agonist counterparts. Each of these antagonists contains a large extension group attached to an agonist or agonist analogue core structure. Importantly, these antagonist compounds were discovered by chance and not designed with a structure-function hypothesis such as the extension principle.

One method of design of a thyroid antagonist using the extension hypothesis is provided below as a teaching example. The three-dimensional structure of the TR-α Dimit complex combined with structure-activity data published in the prior art, especially those reference herein, can be used to establish the following ligand-receptor interactions which are most critical for high-affinity ligand binding.

15 A physical picture of these interactions is shown in **FIG. 6**. The figure describes the isolated essential contacts for ligand binding. Because the ligand is buried in the center of the receptor, the structural spacing between these isolated interactions is also important. Thus, our present knowledge of this system dictates that, for this example, a newly designed ligand for the receptor must contain a thyronine structural skeleton, or two substituted aryl groups joined by a one-atom spacer.

The general structure for an antagonist designed by the extension hypothesis is exemplified in the following general description of the substituents of a TR antagonist (referring to Formula 1): R<sub>1</sub> can have anionic groups such as a carboxylate, phosphonate, phosphate, sulfate or sulfite and is connected to the ring with a 0 to 3 atom linker, comprising one or more C, O, N, S atoms, and preferably a 2 carbon linker. Such R<sub>1</sub> can be optionally substituted with an amine (e.g. -NH<sub>2</sub>). R<sub>3</sub> and R<sub>5</sub> are small hydrophobic groups such as -Br, -I, or -CH<sub>3</sub>. R<sub>3</sub> and R<sub>5</sub> can be the same substituents or different. R<sub>3</sub>' can be a hydrophobic group that may be larger than those of R<sub>3</sub> and R<sub>5</sub>, such as -I, -CH<sub>3</sub>, -isopropyl, -phenyl, -benzyl, 5 and 6 ring heterocycles. R<sub>4</sub>' is a group that can participate in a hydrogen bond as either a donor or acceptor. Such groups include -OH, -NH<sub>2</sub>, and -SH. R<sub>5</sub>' is an important extension group that makes this compound an antagonist. R<sub>5</sub>' can be a long chain alkyl (e.g. 1 to 9 carbons, straight chain or branched), aryl (benzyl, phenyl and substituted benzyl

and phenyl rings (e.g. with halogen, alkyl (1 and 5 carbons) and optionally connected to the ring by a -CH<sub>2</sub>-), heterocycle (e.g. 5 or 6 atoms, preferably 5 carbons and 1 nitrogen, or five carbons), which can optionally include polar (e.g. -OH, -NH<sub>2</sub>, and -SH), cationic (e.g. -NH<sub>3</sub>, N(CH)<sub>3</sub>), or anionic (carboxylate, phosphonate, phosphate 5 or sulfate) groups. R<sub>5</sub>' can also be a polar (e.g. -OH, -NH<sub>2</sub>, and -SH), cationic (e.g. -NH<sub>3</sub>, -N(CH<sub>3</sub>)<sub>3</sub>), and anionic (carboxylate, phosphonate, phosphate or sulfate) groups. X is the spacer group that appropriately positions the two aromatic rings. This group is usually a one-atom spacer, such as O, S, SO, SO<sub>2</sub>, NH, NZ where Z is an alkyl, CH<sub>2</sub>, CHOH, CO, C(CH<sub>3</sub>)OH, and C(CH<sub>3</sub>)(CH<sub>3</sub>). X also may be NR<sub>7</sub>, CHR<sub>7</sub>, CR<sub>7</sub>, R<sub>7</sub>, where R<sub>7</sub>, is an alkyl, aryl or 5- or 6-membered heterocyclic aromatic. R<sub>2</sub>, R<sub>6</sub>, R<sub>2</sub>' and R<sub>6</sub>' can be -F, and -Cl and are preferably H.

A TR ligand can also be described as a substituted phenylated 3,5 diiodo tyrosine with substituted R<sub>5</sub>' and R<sub>3</sub>' groups. R<sub>5</sub>' can be a long chain alkyl (e.g. 4 to 9 carbons, straight chain or branched), aryl (benzyl, phenyl and substituted benzyl and 15 phenyl rings (e.g with halogen, alkyl (1 and 5 carbons) and optionally connected to the ring by a -CH<sub>2</sub>-), heterocycle (e.g. 5 or 6 atoms, preferably 5 carbons and 1 nitrogen, or five carbons), which can optionally include polar (e.g. -OH, -NH<sub>2</sub>, and -SH), cationic (e.g. -NH<sub>3</sub>, N(CH)<sub>3</sub>), or anionic (carboxylate, phosphonate, phosphonate or sulfate) groups. R<sub>5</sub>' can also be a polar (e.g. -OH, -NH<sub>2</sub>, and -SH), cationic (e.g. - NH<sub>3</sub>, N(CH)<sub>3</sub>), and anionic (carboxylate, phosphonate, phosphate or sulfate) groups. R<sub>3</sub>' can be -IsoPr, halogen, -CH<sub>3</sub>, alkyl (1 to 6 carbons) or aryl (benzyl, phenyl and substituted benzyl and phenyl rings (e.g with halogen, alkyl (1 and 5 carbons) and optionally connected to the ring by a -CH<sub>2</sub>-), heterocycle (e.g. 5 or 6 atoms, preferably 5 carbons and 1 nitrogen, or five carbons), which can optionally include polar (e.g. - OH, -NH<sub>2</sub>, and -SH), cationic (e.g. -NH<sub>3</sub>, N(CH)<sub>3</sub>), or anionic (carboxylate, phosphonate, phosphate or sulfate) groups.

A TR antagonist can also be a modified T<sub>3</sub> agonist (having a biphenyl structure) wherein R<sub>5</sub>' is alkyl, aryl, 5- or 6-membered heterocyclic aromatic, heteroalkyl, heteroaryl, arylalkyl, heteroaryl alkyl, polyaromatic, polyheteroaromatic, polar or charged groups, wherein said R<sub>5</sub>' may be substituted with polar or charged groups. The R<sub>5</sub>' groups are defined, as described herein.

Using these methods the ligands of this example preferably have the following properties:

1. The compounds should bind to the TR with high affinity (for example 100 nM).

- 2. The compounds should bind the receptor in the same basic orientation as the natural hormone.
- 5 3. The extension group  $R_5$ ' should project toward the activation helix (C-terminal helix) of the receptor.
  - 4. The appropriate substituent at  $R_5$ ' should perturb the activation helix from its optimal local structure needed for mediating transcription.

Antagonists may also be designed with multiple extensions in order to block 10 more than one aspect of the folding at any time.

TR ligands (e.g. super agonists) can be designed (and synthesized) to enhance the interaction of at least one amino acid with at least one chemical moiety on the ligand's molecular recognition domain. One method is to enhance the charge and polar interactions by replacing the carboxylate of T<sub>3</sub> (R<sub>1</sub> position) with phosphonate, phosphate, sulfate or sulfite. This enhances the interaction with Arg 262, Arg 266 and Arg 228. The interaction of at least one amino acid with at least one chemical moiety on the ligand's molecular recognition domain can also be enhanced by increasing the size of R<sub>1</sub> group to fill the space occupied by water when Dimit is bound (referring to R<sub>1</sub>). Preferably the group has a complementary charge and hydrophobicity to the binding cavity.

Another way of improving the interaction of at least one amino acid with at least one chemical moiety on the ligand's molecular recognition domain is to restrict the conformation of the dihedral angle between the two phenyl rings of the thyronine ligand in solution. In solution the planes of two phenyl rings are orthogonal where the dihedral angle is 90°. In the TR Dimit structure, the dihedral angle is close to 60°. A TR ligand design that fixes the angle between the two phenyl rings will lead to tighter binding. Such a ligand may be made by connecting the R<sub>6</sub>' and the R<sub>5</sub> positions of a thyronine or a substituted thyronine-like biphenyl. The size of the cyclic connection can fix the angle between the two phenyl rings. Referring specifically to Formula 1, 30 the following cyclic modifications are preferred: 1) R<sub>5</sub> is connected to R<sub>6</sub>', 2) R<sub>3</sub> is connected to R<sub>2</sub>' or 3) R<sub>5</sub> is connected to R<sub>6</sub>' and R<sub>3</sub> is connected to R<sub>2</sub>'. The connections can be made by an alkyl or heteroalkyl chain having between 1 to 6 atoms and preferably from 2 to 4 carbon atoms or other atoms. Any position of the heteroalkyl chain can be N, O, P or S. The S and P heteroatoms along said heteroalkyl

chain are in any of their possible oxidative states. The N heteroatom or any carbon along the alkyl or heteroalkyl chain may have one or more Z substituents, wherein Z is alkyl, heteroalkyl, aryl, heteroaryl, 5- or 6-membered heterocyclic aromatic. These compounds can be claimed with the proviso that Formula 1 does not include any prior art compound as of the priority filing date of this application.

The interaction of at least one amino acid with at least one chemical moiety on the ligand's molecular recognition domain can also be enhanced by selecting a chemical modification that fills the unfilled space between a TR ligand and the LBD in the area of the bridging oxygen (such as in T3, Triac or Dimit). Thus, a slighter larger moiety that replaces the ether oxygen can enhance binding. Such a linker may be a mono- or geminal- disubstituted carbon group. A group approximately the same size as oxygen but with greater hydrophobicity is preferred as well as small, hydrophobic groups for the disubstituted carbon.

Compounds of Formula I or derivatives thereof that modulate TR activity also 15 may be designed and selected to interact with a conformationally constrained structural feature of a TR LBD that is conserved among TR LBD isoforms to increase TR-specific selectivity. Conserved structural features of a TR LBD include residues found in equivalent positions of TR LBD isoforms which interact with a conserved structural feature of a compound comprising the biphenyl scaffold  $(\phi - X - \phi)$  or a single 20 phenyl scaffold (φ-X or X-φ) of Formula I. Conformationally constrained structural features of a TR LBD include residues that have their natural flexible conformations fixed by various geometric and physical-chemical constraints, such as local backbone, local side chain, and topological constraints. These types of constraints are exploited to restrict positioning of atoms involved in receptor-ligand recognition and binding. 25 For example, comparison of atomic models of TR LBD isoforms bound to thyronine and thyronine-like ligands reveal that certain residues which contact the ligands are restricted to particular topological shapes and angles of rotation about bonds. These include Met259, Leu276, Leu292, His381, Gly290, Ile221, and Phe401 of TR-α. The corresponding positions in TR-β include Met313, Leu330, Leu346, His435, Gly344, 30 Ile275 and Phe455, respectively.

Selectivity imparted by conformationally constrained features of both the receptor and compound are of particular interest. For example, compounds of Formula I comprising constrained cyclic carbons and substituent groups that interact

with a constrained feature of a TR LBD can be exploited to further increase binding specificity while reducing the potential for cross-over interaction with other receptors. These include hydrophobic and/or hydrophilic contacts between constrained residues of a TR LBD and atomic groups of the following constituents of the compound in 5 reference to Formula I: (i) the biphenyl rings; (ii) the R<sub>3</sub>-substituent; (iii) the R<sub>3</sub>'-substituent; and (iv) the R<sub>4</sub>'-substituent.

For example, contacts to the phenyl moiety comprising the R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>5</sub> and R<sub>6</sub> substituents, i.e., the ring proximal to the polar pocket (the "inner ring"), include a cycle carbon atom that interacts with an atom of a hydrophobic residue of a TR LBD, such as a carbon and oxygen atom of Met259 and a carbon atom of Leu276 of TR-α, or Met313 and Leu330 of TR-β, where the cycle carbon is about 3.0 to 4.0A from the atom of the hydrophobic group. For example, comparison of TR-α complexed with T3 and TR-β complexed with GC-1 reveals the following conserved inner ring contacts:

15				
	<u>Ligand</u>	TR LB	<u>D</u>	_
	T3/Atom	TR-α Residue	Atom	Distance
	C11	Met259	C	3.95
	C11	Met259	O	3.59
20	C11	Met259	CB	3.77
	C7	Leu276	CD2	3.80
	C9	Leu276	CD2	3.70
	GC1/Atom	TR-β Residue	Atom	Distance
25	C11	Met313	C	3.85
	C11	Met313	O	3.41
	C11	Met313	CB	3.79
	C7	Leu330	CD2	3.56
	C9	Leu330	CD2	3.63
30				

Contacts to the phenyl moiety comprising the R<sub>2</sub>', R<sub>3</sub>', R<sub>4</sub>', R<sub>5</sub>' and R<sub>6</sub>' substituents, i.e., the ring distal to the polar pocket (the "outer ring"), include a cyclic carbon atom that interacts with an atom of a hydrophobic residue of a TR LBD, such as a carbon atom of Leu292 of TR-α, or Leu346 of TR-β, where the cyclic carbon atom is about 3.0 to 4.0A from the atom of the hydrophobic residue. For example, comparison of TR-α complexed with T3 and TR-β complexed with GC-1 reveals the following conserved outer ring contacts:

	<u>Ligand</u>	TR LE	BD	_
	T3/Atom	TR-α Residue		Distance
	C6	Leu292	CD2	3.58
	C8	Leu292	CD2	3.50
5	GC1/Atom	TR-β Residue	Atom	Distance
	C6	Leu346	CD2	3.77
	C8	Leu346	CD2	3.80

10 Contacts to the R<sub>3</sub>-substituent include an atom that interacts with a carbon atom of a hydrophobic residue of a TR LBD, such as Ile221 of TR-α, or Ile275 of TR-β, where the R<sub>3</sub>-substituent atom is about 3.0 to 4.0A from the carbon atom of the hydrophobic residue. For example, comparison of TR-α complexed with T3 and TR-β complexed with GC-1 reveals the following conserved R<sub>3</sub>-substituent contacts:

15

	Ligand	TR LBD	<del></del>
	T3/Atom I1	TR-α Residue Atom Ile221 CG1	Distance 4.01
20	GC1/Atom C19	TR-β Residue Atom Ile275 CG1	Distance 3.98

Contacts to the R<sub>3</sub>'-substituent include an atom that interacts with an atom of a hydrophobic or hydrophilic residue of a TR LBD, such as an oxygen atom of Gly290 of TR-α, or Gly344 of TR-β, where the R<sub>3</sub>'-substituent atom is about 3.0 to 4.0A from the atom of the hydrophobic or hydrophilic residue. For example, comparison of TR-α complexed with T3 and TR-β complexed with GC-1 reveals the following conserved R<sub>4</sub>'-substituent, phenolic hydroxyl contacts:

30	<u>Ligand</u>	TR LBD	
	T3/Atom I2	TR-α Residue Atom Gly290 O	Distance 3.50
	GC1/Atom C18	TR-β Residue Atom Gly344 O	Distance 3.60

35

Contacts to the  $R_4$ '-substituent comprising a phenolic hydroxyl include carbon and oxygen atoms that interact with a hydrophobic or hydrophilic residue of a TR LBD, such as a carbon and nitrogen atom of His381 of TR- $\alpha$ , or His435 of TR- $\beta$ ,

where the  $R_4$ '-substituent atom is about 2.0 to 4.0A from an atom of the hydrophobic or hydrophilic residue. For example, comparison of TR- $\alpha$  complexed with T3 and TR- $\beta$  complexed with GC-1 reveals the following conserved  $R_4$ '-substituent, phenolic hydroxyl contacts:

5			
	Ligand	TR LBD	_
	T3/Atom	TR-α Residue Atom	Distance
	C10	His381 CD2 3.97	
	O1	His381 CD2 3.39	
10	O1	His381 CE1 3.82	
	C8	His381 NE2 3.47	
	C10	His381 NE2 3.55	
	O1	His381 NE2 2.70	
	GC1/Atom	TR-β Residue Atom	Distance
15	C10	His435 CD2 3.89	2 15 661100
	O1	His435 CD2 3.64	
	O1	His435 CE1 3.79	
	C8	His435 NE2 3.44	
	C10	His435 NE2 3.33	
20	O1	His435 NE2 2.77	

Contacts to the  $R_4$ '-substituent also may include an atom that interacts with a carbon atom of a hydrophobic residue of a TR LBD, such as Phe401 of TR- $\alpha$ , or 25 Phe455 of TR- $\beta$ , for defining agonist activity, i.e., proper presentation of helix-12 (H12) of the TR LBD following ligand binding. The  $R_4$ '-substituent atom is about 3.0 to 4.0Å from the carbon atom of the hydrophobic group. For example, comparison of TR- $\alpha$  complexed with T3 and TR- $\beta$  complexed with GC-1 reveals the following conserved  $R_4$ '-substituent contacts:

30				
	Ligand	TR LB	D	-
	T3/Atom	TR-α Residue	Atom	Distance
	O1 .	Phe401	CE1	3.52
	O1	Phe401	CZ	3.32
35	GC1/Atom O1 O1	TR-B Residue Phe455 Phe455	Atom CE1 CZ	Distance 3.40 3.22

40 Comparison of atomic models of TR LBD isoforms complexed with the same and/or different ligands therefore facilitates the identification of new compounds that

fit spacially and preferentially into a TR LBD. Modeling, comparison of TR-ligand overlays, and comparison of TR LBD isoforms also permit identification of conformationally conserved structural features of TR LBD/ligand contacts. Exploiting conformational constraints of the LBD-ligand interaction identified by 5 such methods therefore improves the design and identification of new compounds having increased selectivity for binding a particular type of nuclear receptor, such as TR.

#### TR- $\alpha$ and TR- $\beta$ Selectivity for the Thyroid Hormone Receptor

Using the method described herein ligands can be designed that selectively bind to the alpha more than the beta TR or vice versa. The X-ray crystallographic structure of the rat TR-α LBD provides insight into design of such ligands.

The three dimensional structure reveals that the major difference between the TR-α and TR-β in the ligand binding cavity resides in amino acid Ser 277 (with the side group -CH<sub>2</sub>OH) in the rat TR-α and whose corresponding residue is 331, asparagine (with the side group -CH<sub>2</sub>CONH<sub>2</sub>), in the human TR-β. The side chain in human TR-β is larger, charged and has a different hydrogen bonding potential, which would allow the synthesis of compounds that discriminate between this difference. The Ser277 (Asn331 in TR-β) forms part of the polar pocket of the TR LBD, indicating that for TR-α versus TR-β discrimination, ligands can be designed to contain chemical modification of the R1-substitutent with reference to Formula I that exploit this difference.

For example, in the complex of TR-α with Triac, Ser277 does not participate in ligand binding. The absence of a role for Ser277 (Asn331 in beta) is consistent 25 with the equal affinity of Triac for the alpha and beta isoforms, and indirectly supports the contention that alpha/beta selectivity resides in the amino acid substitution Ser277 to Asn331 and its interaction with Arg228. The effect of the amino acid substitution is further evident when the interactions of Asn331 and Arg282 in the structures of the TR-β LBD complexed with GC-1 or Triac are compared with those of Ser277 and Arg228 in the TR-α LBD. In the complex with GC-1, Asn331 forms a hydrogen bond to Arg282, which in turn forms a hydrogen bond with the carboxylate of GC-1, a pattern that resembles the interactions of Ser277 and Arg228 in the complexes of the TR-α LBD complexed with T<sub>3</sub> or Triac.

However, in the complex of TR-β with Triac, Arg282 rotates away from Asn331 and the ligand, instead forming hydrogen bonds to residues Thr287 and Asp291 of H3. Therefore, differences exist between the two isoforms in the conformation of the polar pocket, depending on the nature of the ligand R<sub>1</sub>-substitutent, indicating that certain substituents may interact preferentially with the conformation of a given isoform.

Comparing overlays of various ligands bound to the TR-α versus TR-β LBDs shows the positioning of the ligand to be very similar. Surprisingly, comparison of the volume and area for the TR-α and TR-β LBDs bound by the same or different ligands unexpectedly shows that the cubic space or volume available for 10 accommodating ligand binding by the TR- $\beta$  LBD (645  $\pm$  28.28 Å<sup>3</sup>) is larger and more flexable than that of the TR- $\alpha$  LBD (596.25  $\pm$  7.97 Å<sup>3</sup>) (Table 1). The volume of the ligand binding cavity for TR-α varies over a narrow range of about 8+, with a maximum difference of about 16+. In contrast, the volume of the ligand binding cavity for TR-B differs by nearly 40+ between the complexes with GC-1 and Triac. 15 There also is a difference in the volume of the ligand binding cavity when comparing the same ligand bound to TR- $\alpha$  and TR- $\beta$ . For example, TR- $\alpha$  and TR- $\beta$  complexed with Triac differ in LBD volume by about 36 Å<sup>3</sup>. Comparison of TR-α and TR-β bound to Dimit and GC-1, respectively, which ligands have similar volume/area and superpositioned architecture, show that the difference in LBD volume is about 75 Å<sup>3</sup>. 20 These differences are attributed primarily to variable movement and interaction of side chain groups with ligand substitutents of the phenyl moiety (φ) of the biphenyl scaffold (\$\phi\$-X-\$\phi\$) located proximal to the polar pocket, e.g., R<sub>1</sub>-substituents in reference to Formula I. In contrast, the volume available in the hydrophobic pocket for both the TR-α and TR-β LBDs is substantially the same. For example, binding of 25 Triac to the TR-β LBD displaces the side chain of Arg 282 providing approximately 60 Å<sup>3</sup> in the polar pocket cavity, exposing the polar pocket to bulk solvent exchange. For GC-1 bound to the TR-β LBD, approximately 14 Å<sup>3</sup> is due to side chain motion of Met310, and approximately 44 Å<sup>3</sup> is due to side chain motion of Arg320, the combination of which increases the size of the polar pocket in the TR-β LBD. This 30 extra pliability also may explain the absence of ordered water in the polar pocket of TR-β LBD bound to Triac or GC-1, which is in contrast to the ordered water found in the polar pocket of TR-α LBD bound to Dimit, IpBr2 or T3.

Т	ah	le	1	*

	rΊ	R-α		
	Dimit	Triac	IpBr2	<u>T3</u>
TR LBD (volÅ <sup>3</sup> /areaÅ <sup>2</sup> )	590/456	589/440	601/474	605/472
Ligand (volÅ <sup>3</sup> /areaÅ <sup>2</sup> )	303/314	333/326	326/330	355/346
Complementarity	0.65	0.68	0.66	0.71

	h?	ΓR-β	
	GC-1	Triac	
TR LBD (volÅ <sup>3</sup> /areaÅ <sup>2</sup> )	665/575	625/474	
Ligand (volÅ <sup>3</sup> /areaÅ <sup>2</sup> )	294/310	333/326	
Complementarity	0.61	0.67	

\*TR LBD volume and area are reported in Angstroms measured by GRASP. Complementarity is determined as defined in Lawrence *et al.*, *J. Mol. Biol. 234*:946-950 (1993).

Residue Ser277 in TR-α and the corresponding residue Asn331 of TR-β also contribute to the volumetric differences observed in the polar pockets of these two TR isoforms. And substitution of the Asn331 of hTR-β with serine has the affect of modifying ligand binding affinity of TR-β so that it resembles that of TR-α (See Example 5). Taken together, differences in hydrogen bonding of atoms of the side chain group of Ser277 in TR-α and Asp331 in TR-β extending from the equivalent backbone position in these TR LBDs and the more restricted polar pocket of the TR-α LBD further supports the concept of designing TR LBD isoform-specific ligands 15 having substitutents that fit spacially and preferentially into the polar pocket of either the TR-α or TR-β LBDs. Exploitation of this difference provides an additional means for computational design of isoform-specific TR agonists and antagonists.

In terms of ligand design, these differences mean that for  $\beta$ -selective ligands, some or all of the following differences should be exploited:

- 20 1. The presence of a larger side chain asparagine.
  - 2. The ability of the carbonyl group on the side chain to provide a strong hydrogen bond acceptor.
  - 3. The ability of the amido group on the side chain to provide a two hydrogen bond donors.
- 4. Adjustment of polarity to reorganize the trapped water in the T3 pocket.
  - 5. Greater size and flexibility of the polar pocket.

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In terms of pharmaceutical design, these differences mean that for  $\alpha$ -selective ligands, some or all of the following differences should be exploited:

- 1. The presence of a smaller side group.
- 2. The ability of the hydroxyl on the -CH<sub>2</sub>OH side group carbonyl group on the side chain to provide a weak hydrogen donor.
- 3. Adjustment of polarity to reorganize the trapped water in the T3 pocket.
- 4. Smaller size and limited flexibility of the polar pocket.

In both cases these differences can be exploited in a number of ways. For example, they can also be used with a software set for construction of novel organic molecules such as LUDI from Biosym-MSI. An example of designing TR-β selective ligands is increasing the polarity of a ligand substituent located in the polar pocket of a TR LBD through addition of one or more ligand groups having a formal negative charge and/or negative dipole charge that interacts with a formal positive charge and/or positive dipole charge of a group in the polar pocket of the LBD. This exploits preferential interactions, such as with the additional positive charge contributed by Asn 331 in TR-β. Another example of a TR-β selective ligand is one that comprises one or more groups which fit spacially into the TR-β LBD polar pocket. This exploits spacial differences between TR LBD isoforms, such as the larger and more flexible polar pocket of TR-β.

#### METHODS OF TREATMENT

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The compounds of Formula 1 can be useful in medical treatments and exhibit biological activity which can be demonstrated in the following tests:

(GPDH:EC 1.1.99.5). This assay is particularly useful since in certain species e.g. rats it is induced specifically by thyroid hormones and thyromimetics in a close-related manner in responsive tissues e.g. liver, kidney and the heart (Westerfield, W.W., Richert, D.A. and Ruegamer, W.R., *Endocrinology* (1965) 77:802). The assay allows direct measurement in rates of a thyroid hormone-like effect of compounds and in particular allows measurement of the direct thyroid hormone-like effect on the heart. Other measurements included parameters such as heart rate and cardiac

enzymes including Ca<sup>++</sup> ATPase, Na<sup>++</sup>/K<sup>+</sup> ATPase, myosin isoforms and specific liver enzymes;

- (ii) the elevation of basal metabolic rate as measured by the increase in whole body oxygen consumption (see e.g., Barker *et al.*, *Ann. N. Y. Acad. Sci.*, (1960) 5 86:545-562);
  - (iii) the stimulation of the rate of beating of atria isolated from animals previously dosed with thyromimetrics (see e.g., Stephan *et al.*, *Biochem. Pharmacol.* (1992) 13:1969-1974; Yokoyama *et al.*, *J. Med. Chem.*, (1995) 38:695-707);
- (iv) the change in total plasma cholesterol levels as determined using a 10 cholesterol oxidase kit (for example, the Merck CHOD iodine colorimetric kit. see also, Stephan *et al.* (1992));
- (v) the measurement of LDL (low density lipoprotein) and HDL (high density lipoprotein) cholesterol in lipoprotein fractions separated by ultracentrifugation; and p (vi) the change in total plasma triglyceride levels as determined using enzymatic color tests, for example the Merck System GPO-PAP method.

The compounds of Formula 1 can be found to exhibit selective thyromimetic activity in these tests,

- (a) by increasing the metabolic rate of test animals, and raising hepatic 20 GPDH levels at doses which do not significantly modify cardiac GPDH levels.
  - (b) by lowering plasma cholesterol and triglyceride levels, and the ratio of LDL to HDL cholesterol at doses which do not significantly modify cardiac GPDH levels.

The compounds of Formula 1 may therefore be used in therapy, in the 25 treatment of conditions which can be alleviated by compounds which selectively mimic the effects of thyroid hormones in certain tissues whilst having little or no direct thyromimetic effect on the heart. For example, compounds of Formula 1 which raise hepatic GPDH levels and metabolic rate at doses which do not significantly modify cardiac GPDH levels are indicated in the treatment of obesity.

Agonists of Formula 1 will lower total plasma cholesterol, the ratio of LDL-cholesterol to HDL-cholesterol and triglyceride levels at doses which do not significantly modify cardiac GPDH levels are indicated for use as general antihyperlipidaemic (antihyperlipoproteinaemic) agents i.e. in the treatment of patients having elevated plasma lipid (cholesterol and triglyceride) levels. In

addition, in view of this effect on plasma cholesterol and triglyceride, they are also indicated for use as specific anti-hypercholesterolemic and anti-hypertriglyceridaemic agents.

Patients having elevated plasma lipid levels are considered at risk of developing coronary heart disease or other manifestations of atherosclerosis as a result of their high plasma cholesterol and/or triglyceride concentrations. Further, since LDL-cholesterol is believed to be the lipoprotein which induces atherosclerosis, and HDL-cholesterol believed to transport cholesterol from blood vessel walls to the liver and to prevent the build up of atherosclerotic plaque, anti-hyperlipidemic agents which lower the ratio of LDL-cholesterol to HDL cholesterol are indicated as anti-atherosclerotic agents, herein incorporated by reference U.S. patents 4,826,876 and 5,466,861.

The present invention also provides a method of producing selective thyromimetic activity in certain tissues except the heart which comprises administering to an animal in need thereof an effective amount to produce said activity of a compound of Formula 1 or a pharmaceutically acceptable salt thereof.

The present invention also relates to a method of lowering plasma lipid levels and a method of lowering the ratio of LDL-cholesterol to HDL-cholesterol levels by suitably administering a compound of this invention or a pharmaceutically acceptable 20 sale thereof.

In addition, compounds of Formula 1 may be indicated in thyroid hormone replacement therapy in patients with compromised cardiac function.

In therapeutic use the compounds of the present invention are usually administered in a standard pharmaceutical composition.

The present invention therefore provides in a further aspect pharmaceutical compositions comprising a compound of Formula 1 or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier. Such compositions include those suitable for oral, parenteral or rectal administration.

#### PHARMACEUTICAL COMPOSITIONS

Compounds of Formula 1 and their pharmaceutically acceptable salts which are active when given orally can be formulated as liquids for example syrups, 5 suspensions or emulsions, tablets, capsules and lozenges.

A liquid composition will generally consist of a suspension or solution of the compound or pharmaceutically acceptable salt in a suitable liquid carrier(s), for example ethanol, glycerine, sorbitol, non-aqueous solvent such as polyethylene glycol, oils or water, with a suspending agent, preservative, surfactant, wetting agent, 10 flavoring or coloring agent. Alternatively, a liquid formulation can be prepared from a reconstitutable powder.

For example a powder containing active compound, suspending agent, sucrose and a sweetener can be reconstituted with water to form a suspension; and a syrup can be prepared from a powder containing active ingredient, sucrose and a sweetener.

A composition in the form of a tablet can be prepared using any suitable pharmaceutical carrier(s) routinely used for preparing solid compositions. Examples of such carriers include magnesium stearate, starch, lactose, sucrose, microcrystalline cellulose and binders, for example polyvinylpyrrolidone. The tablet can also be provided with a color film coating, or color included as part of the carrier(s). In addition, active compound can be formulated in a controlled release dosage form as a tablet comprising a hydrophilic or hydrophobic matrix.

A composition in the form of a capsule can be prepared using routine encapsulation procedures, for example by incorporation of active compound and excipients into a hard gelatin capsule. Alternatively, a semi-solid matrix of active compound and high molecular weight polyethylene glycol can be prepared and filled into a hard gelatin capsule; or a solution of active compound in polyethylene glycol or a suspension in edible oil, for example liquid paraffin or fractionated coconut oil can be prepared and filled into a soft gelatin capsule. Compound of Formula 1 and their pharmaceutically acceptable salts which are active when given parenterally can be 30 formulated for intramuscular or intravenous administration.

A typical composition for intra-muscular administration will consist of a suspension or solution of active ingredient in an oil, for example arachis oil or sesame oil. A typical composition for intravenous administration will consist of a sterile isotonic aqueous solution containing, for example active ingredient, dextrose, sodium

chloride, a co-solvent, for example polyethylene glycol and, optionally, a chelating agent, for example ethylenediamine tetracetic acid and an anti-oxidant, for example, sodium metabisulphite. Alternatively, the solution can be freeze dried and then reconstituted with a suitable solvent just prior to administration.

Compounds of structure (1) and their pharmaceutically acceptable salts which are active on rectal administration can be formulated as suppositories. A typical suppository formulation will generally consist of active ingredient with a binding and/or lubricating agent such as a gelatin or cocoa butter or other low melting vegetable or synthetic wax or fat.

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10 Compounds of Formula 1 and their pharmaceutically acceptable salts which are active on topical administration can be formulated as transdermal compositions. Such compositions include, for example, a backing, active compound reservoir, a control membrane, liner and contact adhesive.

The typical daily dose of a compound of Formula 1 varies according to 15 individual needs, the condition to be treated and with the route of administration. Suitable doses are in the general range of from 0.001 to 10 mg/kg bodyweight of the recipient per day.

Within this general dosage range, doses can be chosen at which the compounds of Formula 1 lower plasma cholesterol levels and raise metabolic rate 20 with little or no direct effect on the heart. In general, but not exclusively, such doses will be in the range of from lower doese (0.001 to 0.5 mg/kg) to higher doses (0.5 to 10 mg/kg).

In addition, within the general dose range, doses can be chosen at which the compounds of Formula 1 lower plasma cholesterol levels and have little or no effect 25 on the heart without raising metabolic rate. In general, but not exclusively, such doses will be in the range of from 0.001 to 0.5 mg/kg.

It is to be understood that the 2 sub ranges noted above are not mutually exclusive and that the particular activity encountered at a particular dose will depend on the nature of the compound of Formula 1 used.

Preferably, the compound of Formula 1 is in unit dosage form, for example, a tablet or a capsule so that the patient may self-administer a single dose. In general, unit doses contain in the range of from 0.05-100 mg of a compound of Formula 1. Preferred unit doses contain from 0.05 to 10 mg of a compound of Formula 1.

The active ingredient may be administered from 1 to 6 times a day. Thus daily doses are in general in the range of from 0.05 to 600 mg per day. Preferably, daily doses are in the range of from 0.05 to 100 mg per day. Most preferably from 0.05 to 5 mg per day.

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#### **EXAMPLES**

#### **EXAMPLE 1 - SYNTHESIS OF TR LIGANDS**

Many TR ligands are known in the art, including T4 (thyroxine), T3, T2 and TS-9. See Jorgensen, Thyroid Hormones and Analogs, in *Hormonal Proteins and* 10 *Peptides, Thyroid Hormones* 107-204 (Choh Hao Li ed., 1978), incorporated by reference herein.

The syntheses of several TR ligands are described below.

#### Synthesis of TS1, TS2, TS3, TS4, TS5

TS1, TS2, TS3, TS4 and TS5 and analogs thereof can all be prepared by simple acylation of the nitrogen atom of any thyronine analog, including T3 (3,5,3'-triiodo-L-thyronine), T4 (thyroxine) and 3,5-diiodothyronine. TS1 and TS2 are synthesized by reacting T3 with Ph<sub>2</sub>CHCO<sub>2</sub>NHS (N-hydroxy succinimide-2,2-diphenylacetate) and C<sub>16</sub>H<sub>33</sub>CO<sub>2</sub>NHS, respectively. TS3 is synthesized by reacting T3 with FMOC-Cl (fluorenylmethyloxycarbonylchloride). TS4 is synthesized by reacting T3 with tBOC<sub>2</sub>O (tBOC anhydride or di-t-butyldicarbonate). TS5, which differs from TS1-4 by having a -H instead of an -I at the R'<sub>3</sub> position, is synthesized by reacting 3,5-diiodothyronine with tBOC<sub>2</sub>O. The general reaction scheme for TS1, TS2, TS3, TS4 and TS5 is depicted in **FIG. 11.** It should be noted that in the reaction scheme, both TS5 and its precursor both have a hydrogen rather than an iodine at the R'<sub>3</sub> position.

#### Synthesis of TS6 and TS7

TS6 is synthesized by reacting TS5 with paranitrophenylisocyanate. TS7 is synthesized by reacting TS6 with TFA (trifluoroacetic acid), which cleaves the tBOC group. These reactions are simple organic synthesis reactions that can be performed by anyone of ordinary skill in the art. The synthetic scheme for TS6 and TS7 is diagrammed in **FIG. 12.** 

#### Synthesis of TS8

TS8 is synthesized by reacting TS5 with Ph<sub>2</sub>CHNH<sub>2</sub> (diphenylmethylamine) in the presence of triethylamine and any amide forming condensing reagent, such as 5 TBTU (hydroxybenztriazoleuronium tetrafluoroborate) or HBTU (hydroxybenztriazoleuronium hexafluorophosphate). The synthesis scheme for TS8 is depicted in FIG. 13.

#### SYNTHESIS OF 3,5-DIIODO-3'ISOPROPYLTHYRONINE DERIVATIVES

For designing a class of antagonists, it is important to have a hydrophobic group at the 3' position as well as an extension at the 5' position. Preferred hydrophobic groups at the 3' position include: methyl, benzyl, phenyl, iodo, and heterocyclic structures. The synthesis of a 3,5-diiodo-3'-isopropyl-5'-substituted thyronine is described below. The example provided describes the specific steps for synthesizing the TS10 compound, but this general reaction scheme can be used by one of ordinary skill in the art to synthesize any number of 3,5,-diiodo-3'-isopropyl-5'-substituted thyronine derivatives, which are characterized by having an extension at the 5' position. Additional compounds of this class can be synthesized using known organic synthesis techniques.

The synthesis of TS10 is described below and is depicted in **FIG. 14.**Numbers used in the reaction scheme for TS10 indicating the reaction product for each step are in parentheses.

2-Formyl-6-isopropylanisole (1): 2-formyl-6-isopropylanisole (10.0 g, 61 mmol), as made by Casiraghi, *et al.* JCS Perkin I, 1862 (1980) (incorporated by reference), is added dropwise to a suspension of sodium hydride (3.7 g, 153 mmol) in 50 mL THF and 50 mL of DMF in a round bottom flask. The addition generates an exothermic reaction and formation of a gray solid. Methyl iodide (26.0 g, 183 mmol) is then added dropwise and the reaction mixture is stirred at room temperature for 5 hours. The reaction mixture is quenched with 20 mL of water, then poured into 500 mL of water, and is extracted with ether (2 x 300 mL). The ether layers are combined, washed with water (5 x 1000 mL), dried over magnesium sulfate and concentrated in vacuo to provide 10.2 g (94%) of the title compound, with the following <sup>1</sup>H NMR (CDCl<sub>3</sub>) properties: d 10.30 (s, 1H), 7.63 (d, 1H, J=3 Hz), 7.50

(d, 1H, J=3 Hz), 7.13 (t, 1H, J=3 Hz), 3.81 (s, 3H), 3.31 (heptet, 1H, J=7.5 Hz), 1.19 (d, 6H, J=7.5 Hz).

2-(2-Hydroxynonyl)-6-isopropylanisole (not shown in scheme):

5 Octylmagnesium chloride (8.4 mL, 16.9 mmol, 2.0 M) is added dropwise to a solution of 1 (1.5 g, 8.4 mmol) in 10 mL THF at -78°C. The reaction mixture is stirred for 2 hours with warming to room temperature. The reaction mixture is diluted with 50 mL ether and poured into 50 mL water. The ether layer is washed with brine (1 x 50 mL), dried over sodium sulfate, and concentrated in vacuo. Flash chromatography (silica 10 gel, 10% ether/hexane → 15% ether/hexane) provides 734 mg (30%) of the title compound with the following ¹H NMR (CDCl₃) properties: d 7.33-7.10 (m, 3H), 5.00 (br. s, 1H), 3.81 (s, 3H), 3.33 (heptet, 1H, J=7 Hz) 1.90-1.19 (m, 14H), 0.86 (t, 3H, J=6.5 Hz); HRMS (EI), found: 292.2404; calc'd: 292.2402.

2-nonyl-6-isopropylanisole (2): Compound 2 (663 mg, 2.3 mmol) is dissolved in solution of 5 mL ethanol and 5 mL acetic acid, and a spatula tip of palladium on carbon catalyst is added. The reaction mixture is then charged with hydrogen gas (using a simple balloon and needle) and the mixture is stirred at room temperature overnight. The next day, the reaction mixture is poured into ether (100 mL) and the ether layer is extracted with saturated sodium bicarbonate (3 x 100 mL). The ether layer is dried over sodium sulfate and concentrated *in vacuo* to provide 581 mg (91%) of (2) with the following <sup>1</sup>H NMR (CDCl<sub>3</sub>) properties: d 7.14-7.00 (m, 3H), 3.75 (s, 3H), 3.36 (heptet, 1H, J=6.8 Hz), 2.63 (t, 2H, J=7.5 Hz), 1.68-1.15 (m, 14H), 0.86 (t, 3H, J=5.5 Hz); HRMS (EI), mass found: 276.2459; calculated: 276.2453.

Thyronine adduct (4): Fuming nitric acid (0.071 mL) is added to 0.184 mL acetic anhydride chilled to -5°C. Iodine (66 mg) is added to this mixture followed by trifluoroacetic acid (0.124 mL). This mixture is stirred for 1 hour with warming to room temperature, at which point all of the iodine is dissolved. The reaction mixture was then concentrated *in vacuo* to provide an oily semi-solid material. The residue was dissolved in 0.7 mL of acetic anhydride and cooled to -20°C. A solution of anisole (2) (581 mg, 2.1 mmol) in 1.2 mL acetic anhydride and 0.58 mL TFA is added dropwise. The reaction mixture is stirred at -20° for 1 hour, then stirred overnight with warming to room temperature. The reaction mixture is partitioned between water and methylene chloride. The methylene chloride layer is dried over sodium

sulfate and concentrated *in vacuo* to provide the iodonium salt (3) as an oil. This material is not purified or characterized, and is directly introduced into the coupling reaction.

N-Trifluoroacetyl-3,5-diiodotyrosine methyl ester (552 mg, 1.0 mmol) prepared according to the procedure of N. Lewis and P. Wallbank, *Synthesis* 1103 (1987) (incorporated by reference) and all of the crude iodonium salt (3) from above is dissolved in 5 mL of anhydrous methanol. Diazabicyclo[5.4.0]undecane (DBU) (183 mg, 1.2 mmol) and a spatula tip of copper-bronze are added and the resulting mixture is stirred at room temperature overnight. The next day, the reaction mixture is filtered, and the filtrate is concentrated *in vacuo*. The crude residue is purified by flash chromatography (silica gel, 10% ethyl acetate/hexane) to provide 30 mg (4%) of the protected thyronine adduct (4).

Deprotected thyronine (TS10): The protected thyronine 4 (30 mg, 0.04 mmol) is dissolved in a mixture of 2.25 mL acetic acid and 2.25 mL 49% hydrobromic acid.

15 The reaction mixture is heated to reflux for 5 hours. The reaction mixture is cooled to room temperature, and the solvents are removed *in vacuo*. Water is added to triturate the oily residue into a gray solid. This solid material is filtered, washed with water, and dried over P<sub>2</sub>O<sub>5</sub> *in vacuo* to provide 24 mg (81%) of the title compound, TS10, with the following <sup>1</sup>H NMR (CDCl<sub>3</sub>) properties: d 7.57 (s, 1H), 6.86 (s, 1H), 6.45 (s, 1H), 6.34 (s, 1H), 4.81 (m, 1H), 3.86 (s, 3H), 3.71 (s, 3H), 3.33-3.05 (m, 3H), 2.58-2.47 (m, 2H), 1.62-0.76 (m, 23H); MS (LSIMS): M<sup>+</sup> = 817.0.

As mentioned above, this reaction scheme can be modified by one of ordinary skill in the art to synthesize a class of compounds characterized by 3,5-diiodo-3'isopropylthyronine derivatives, wherein (1) the 3' isopropyl group can be replaced with a hydrophobic group, including methyl, benzyl, phenyl, iodo, and heterocyclic structures, and (2) a wide variety of chemical structures can be incorporated at the 5' position, including alkyl groups, planar aryl, heterocyclic groups, or polar and/or charged groups.

The aldehyde (1) in the above reaction scheme is a versatile synthetic 30 intermediate which allows for the attachment of a variety of chemical moieties to the 5' position of the final thyronine derivative. In addition, a variety of chemical reactions can be used to attach the chemical moieties. These reactions are well known in the art and include organometallic additions to the aldehyde (including Grignard reagents, organolithiums, etc.), reductive amination reactions of the aldehyde with a

primary or secondary amine, and Wittig olefination reactions with a phosphorous ylid or stabilized phosphonate anion. Other possibilities include reduction of the aldehyde to a benzyl alcohol allowing for etherification reactions at the 5' position. As mentioned above, these methods allow for a wide variety of chemical structures to be incorporated at the 5' position of the final thyronine derivative, including alkyl groups, planar aryl, heterocyclic groups or polar and/or charged groups.

Synthesis of 3, 5-dibromo-4-(3',5'-diisopropyl-4'-hydroxyphenoxy) benzoic acid (Compound 11).

- (a) A mixture of 2,6-diisopropyl phenol (20 g, 0.11 mol), potassium carbonate (62 g, 0.45 mol), acetone (160 ml) and methyl iodide (28 ml, 0.45 mole) is refluxed for three days. The reaction mixture is filtered through celite, evaporated, dissolved in ether, washed twice with 1M sodium hydroxide, dried over magnesium sulphate and concentrated to afford 15.1 g (0.08 mol, 70%) of 2,6-diisopropyl anisole as a 20 slightly yellow oil.
- (b) Fuming nitric acid (12.4 ml, 265 mmol) is added dropwise to 31.4 ml of acetic anhydride which is cooled in a dry ice/carbon tetrachloride bath. Iodine 11.3 g, 44.4 mmol) is added in one portion followed by dropwise addition of trifluoroacetic acid (20.5 ml, 266 mmole). The reaction mixture is stirred at room temperature until all the iodine is dissolved. Nitrogen oxides are removed by flushing nitrogen into the vessel. The reaction mixture is concentrated, the residue is dissolved in 126 ml of acetic anhydride and is cooled in a dry ice/carbon tetrachloride bath. To the stirred solution 2,6-diisopropylanisole (51 g, 266 mmol) in 150 ml of acetic anhydride and 22.6 ml of trifluoroacetic acid is added dropwise. The reaction mixture is left to stand at room temperature over night and then is concentrated. The residue is taken up in 150 ml of methanol and treated with 150 ml of 10% aqueous sodium bisulfite solution and 1 liter of 2M sodium borotetrafluoride solution. After the precipitate aggregates, petroleum ether is added and the supernatant is decanted. The precipitate is triturated with petroleum ether, filtered, washed with petroleum ether and dried at room

temperature in vacuo. This affords 34 g (57 mmol, 65%) of bis(3,5-diisopropyl-4-methoxyphenyl)iodonium tetrafluoroborate as a white solid.

- (c) To a stirred solution of 3,5-dibromo-4-hydroxybenzoic acid (12 g, 40.5 mmol) in 250 ml of methanol, thionyl chloride (3 ml) is added dropwise. The 5 reaction mixture is refluxed for five days, water is added and the precipitated product is filtered off. The residue is dissolved in ethyl acetate. From the aqueous phase, methanol is removed by concentration. The aqueous phase is then saturated with sodium chloride, and extracted with ethyl acetate. The combined organic phases are dried over magnesium sulphate, filtered and concentrated. This gives 12.5 g (40.5 mmol, 100%) of 3,5-dibromo-4-hydroxymethyl benzoate as a white crystalline solid.
- The products obtained in steps b and c are reacted with each other according to the following protocol. To bis(3,5-diisopropyl-4methoxyphenyl)iodonium tetrafluoroborate (2.86 g, 4.8 mmole) and copper bronze (0.42 g, 6.4 mmole) in 7 ml. of dichloromethane at 0°C is added dropwise a solution 15 of 3,5-dibromo-4-hydroxymethyl benzoate (1.0 g, 3.2 mmole) and triethylamine (0.36 g, 3.5 mmole) in 5 ml of dichloromethane. The reaction mixture is stirred in the dark for eight days and then is filtered through celite. The filtrate is concentrated and the residue is purified by column chromatography (silica gel, 97:3 petroleum ether/ethyl acetate) to give 0.62 g (1.2 mmole, 39%) of 3,5-dibromo-4-(3',5'-diisopropyl-4'-20 methoxyphenoxy)methyl benzoate as a solid.
- (e) The product from step d (0.2 g, 0.4 mmole) is dissolved in 2 ml. dichloromethane, is put under nitrogen and is cooled at -40°C. To the stirred solution is added 1M BBr<sub>3</sub> (1.2 ml, 1.2 mmole) dropwise. The reaction mixture is allowed to reach room temperature and then is left over night. It is cooled to 0°C and then 25 hydrolyzed with water. Dichloromethane is removed by concentration and the aqueous phase is extracted with ethyl acetate. The organic phase is washed with 1M hydrochloric acid and brine. Then it is dried over magnesium sulphate, filtered and chromatographed (silica, 96:3.6:0.4 concentrated. The residue is dichloromethane/methanol/acetic acid) producing 93 mg (0.2 mmole, 51%) of 3,5-30 dibromo-4-(3',5'-diisopropyl-4'-hydroxyphenoxy)benzoic acid as a white solid. <sup>1</sup>H nmr (CDCl<sub>3</sub>)  $\delta$  1.23 (d, 12H, methyl), 3.11 (m, 2H, CH), 6.50 (s, 2H, 2,6-H) 8.33 (s, 2H, 2',6'-H).

Synthesis of addition ligands are described in U.S. Serial No. 08/877,792, filed June 18, 1997 which is herein incorporated in its entirety by reference.

**TABLE 2** and **FIG. 15** depict the structures of several TR ligands in reference to Formula I.

TABLE 2

Cmpd	R <sub>3</sub>	$R_4$	R <sub>5</sub>	R' <sub>3</sub>	R' <sub>4</sub>	R'5	R <sub>1</sub>
*T <sub>3</sub>	-I	-O-	-I	-I	-ОН	-H	-CH₂CH(NH₂)CO₂H
*T <sub>4</sub>	-I	-0-	-I	I-	-OH	-I	-CH₂CH(NH₂)CO₂H
TS1	-I	-O-	-I	-I	-OH	-Н	-CH₂CH[NHCOCHφ₂]CO₂H
TS2	-I	-0-	-I	-I	-OH	-H	-CH <sub>2</sub> CH[NHCO(CH <sub>2</sub> ) <sub>15</sub> CH <sub>3</sub> ]CO <sub>2</sub> H
TS3	-l	-O-	-1	-I	-OH	-H	-CH2CH[NH-FMOC]CO2H
TS4	-I	-0-	-I	-I	-OH	-H	-CH₂CH[NH-tBOC]CO₂H
TS5	-I	-O-	-I	-H	-ОН	-H	-CH <sub>2</sub> CH[NH-tBOC]CO <sub>2</sub> H
TS6	-I	-0-	-I	-H	-OC(O)NH=Ø <sub>p</sub> NO <sub>2</sub>	-Н	-CH <sub>2</sub> CH[NH-tBOC]CO <sub>2</sub> H
TS7	-I	-0-	-I	-I	- OC(O)NH=NHØNO <sub>2</sub>	-H	-CH₂CH(NH₂)CO₂H
TS8	-I	-O-	-I	-H	-NH-CHØØ	-H	-CH₂CH[NH-tBOC]CO₂H
TS9	-I	-O-	-I	-IsoPr	-ОН	-H	-CH <sub>2</sub> CH(NH <sub>2</sub> )CO <sub>2</sub> H
TS10	-I	-0-	-I	-lsoPr	-ОН	-(CH) <sub>8</sub> - CH <sub>3</sub>	-CH₂CH(NH₂)CO₂H

Prior Art Compound

-Ø: phenyl

-ØpNO<sub>2</sub>: para nitro phenyl

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#### EXAMPLE 2 - RECEPTOR BINDING ASSAYS OF TR LIGANDS

To test the ability of synthesized TR ligands to bind to a thyroid receptor (TR), the binding affinity of a TR ligand for TR is assayed using TR's prepared from rat liver nuclei and [125]T<sub>3</sub> as described in J.D. Apriletti, J.B. Baxter, and T.N. Lavin, J. 15 *Biol. Chem.*, 263: 9409-9417 (1988). The apparent Kd's are calculated using the method described by Apriletti (1995) and Apriletti (1988). The apparent Kd's are presented in **TABLE 3**. The apparent Kd's (App.Kd) are determined in the presence

of the sample to be assayed, 1 nM [<sup>125</sup>I]T<sub>3</sub>, and 50Tg/ml core histones, in buffer E (400 mM KCl, 200 mM potassium phosphate, pH 8.0, 0.5 mM EDTA, 1 mM MgCl<sub>2</sub>, 10% glycerol, 1 mM DTT) in a volume of 0.21 ml. After incubation overnight at 4°C, 0.2 ml of the incubation mixture is loaded onto a Quick-Sep Sephadex G-25 column 5 (2.7 x 0.9 cm, 1.7 ml bed volume) equilibrated with buffer E. The excluded peak of protein-bound [<sup>125</sup>I]T<sub>3</sub> is eluted with 1 ml of buffer E, collected in a test tube, and counted. Specific T<sub>3</sub> binding is calculated by subtracting nonspecific binding from total binding.

TABLE 3

Compound	App.Kd(nM)	Coactivation Assay RIP-140	EC <sub>50</sub> (M)
T <sub>3</sub>	0.06	+	10-10
T <sub>4</sub>	2	+	10-9
TS1	4	+	10-7
TS2	1400	nd	nd
TS3	4	+	10 <sup>-8</sup>
TS4	8	+	nd
TS5	220	+	10 <sup>-6</sup>
TS6	>10000	nd	nd
TS7	260	+	10-7
TS8	6000	nd	nd
TS9	1	+	10 <sup>-10</sup>
TS10	400	+	10-6

10

+: RIP-140 Binding

-: RIP-140 Binding

nd: Not Determined

#### EXAMPLE 3 - INCREASED NUCLEAR PROTEIN COACTIVATION BY TR LIGANDS

To test the ability of TR ligands to activate the binding of TR to the nuclear activation protein RIP-140 (a nuclear protein that can bind to nuclear receptors, such as the estrogen receptor), a TR ligand is liganded to TR and then incubated with RIP-140 as described in V. Cavailles, *et al.*, *EMBO J.*, 14(15):3741-3751 (1995), which is incorporated by reference herein. In this assay, <sup>35</sup>S-RIP-140 protein binds to liganded TR but not unliganded TR. Many TR <sup>35</sup>S ligands can activate RIP-140 binding as shown in **TABLE 3**.

#### 10 Example 4 - TR LIGAND BINDING AND TR ACTIVATION IN CULTURED CELLS

To test TR activation of transcription in a cellular environment, TR ligands are assayed for their ability to activate a reporter gene, chloramphenicol transferase ("CAT"), which has a TR DNA binding sequence operatively linked to it. Either GC or L937 cells (available from the ATCC) can be used, respectively). In such assays, a 15 TR ligand crosses the cell membrane, binds to the TR, and activates the TR, which in turn activates gene transcription of the CAT by binding the TR DNA binding region upstream of the CAT gene. The effective concentration for half maximal gene activation (EC<sub>50</sub>) is determined by assaying CAT gene activation at various concentrations as described herein and in the literature. The results of CAT gene 20 activation experiments are shown in **TABLE 3**.

#### **CAT GENE ACTIVATION ASSAYS**

Functional response to thyroid hormone (3,5,3'-triiodo-L-thyronine, T<sub>3</sub>) and TR ligands is assessed either in a rat pituitary cell line, GC cells, that contain endogenous thyroid hormone receptors (TRs) or U937 cells that contain exogenous TRs expressed as known in the art. GC cells are grown in 10-cm dishes in RPMI 1640 with 10% newborn bovine serum, 2 mM glutamine, 50 units/ml penicillin and 50 Tg/ml streptomycin. For transfections, cells are trypsinized, resuspended in buffer (PBS, 0.1% glucose) and mixed with a TREtkCAT plasmid (10 mg) or phage in 0.5 ml buffer (15±5 million cells) and electroporated using a Bio-Rad gene pulser at 0.33 kvolts and 960 mF. The TREtkCAT plasmid contains two copies of a T<sub>3</sub> response element (AGGTCAcaggAGGTCA) cloned in the Hind III site of the pUC19 polylinker immediately upstream of a minimal (-32/+45) thymidine kinase promoter

linked to CAT (tkCAT) coding sequences. After electroporation, cells are pooled in growth medium (RPMI with 10% charcoal-treated, hormone stripped, newborn bovine serum), plated in 6-well dishes and treated with either ethanol or hormone. CAT activity is determined 24 hours later as described D. C. Leitman, R. C. J. 8 Ribeiro, E. R. Mackow, J. D. Baxter, B. L. West, *J. Biol. Chem.* 266, 9343 (1991), which is incorporated by reference herein.

### EFFECT OF TS-10 ON THE TRANSCRIPTIONAL REGULATION OF THE DR4-ALP REPORTER GENE IN THE PRESENCE OR ABSENCE OF T3.

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Characteristics of the TRAF cells: TRAFa1 are CHO K1 cells stably transformed with an expression vector encoding the human thyroid hormone receptor α1 and a DR4,ALP reporter vector; TRAFb1 are CHO K1 cells stably transformed with an expression vector encoding the human thyroid hormone receptor β1 and a 15 DR4-ALP reporter vector.

# Interpretation of the effect of compound TS-10 on the transcriptional regulation of the DR4-ALP reporter gene in the presence or absence of T3.

TRAFa1 reporter cells: TS-10 alone (open circles) induces a partial activation of the expression of the ALP reporter protein amounting to approximately 27% of the maximal effect by the natural thyroid hormone T3. In the presence of T3 (filled circles), TS-10 has a weak antagonistic effect. The EC50 concentration for the agonistic effect of TS-10 and the EC50 concentration for its T3 antagonistic effect, respectively, is indicated in FIG. 18.

In **FIG. 18**, open and filled circles with dotted lines show the dose-dependent effect of TS-10/T3 on the toxicity marker (MTS/PMS), reduction of tetrazolium salt in the mitochondria, displayed on the right y-axis as optical density. There is no 30 obvious toxic effect of TS-10 on the MTS-PMS marker but there is a clear effect on the morphology of the cells, as can be seen under the light microscope, at the highest concentration of TS-10 (32 mM) both in the absence and presence of T3, respectively (not shown in the figure).

TRAFb1 reporter cells: TS-10 alone (open circles) induces a partial activation of the expression of the ALP reporter protein amounting to approximately 35% of the maximal effect by T3. The EC50 concentration for the agonistic effect of 5 TS-10 is indicated in FIG. 19. In the presence of T3 (filled circles), TS-10 shows, if anything, a slight potentiation of the T3 effect on the expression of the ALP reporter protein. The T3 inhibitory effect of TS-10 at its highest concentration used (32 mM) is a toxic effect rather than T3 antagonism.

In **FIG. 19**, open and filled circles with dotted lines show the dose-dependent effect of TS-10/T3 on the toxicity marker (MTS/PMS), reduction of tetrazolium salt in the mitochondria, displayed on the right y-axis as optical density. There is no obvious toxic effect of TS-10 on the MTS-PMS marker but a clear effect on the morphology of the cells can be observed, under the light microscope, at the highest concentration of TS-10 (32 mM) both in the absence and presence of T3, respectively (not shown in the figure).

HepG2 (HAF18) reporter cells: TS-10 alone (open circles) induces a partial activation of the expression of the ALP reporter protein amounting to slightly more 20 than 50% of the maximal effect by T3. The EC50 concentration for the agonistic effect of TS-10 is indicated in FIG. 20. In the presence of T3 (filled circles), TS-10 shows no effect i.e. no T3 antagonism nor potentiation/additive effect to T3. Open and filled circles with dotted lines show the dose-dependent effect of TS-10/T3 on the toxicity marker (MTS/PMS), reduction of tetrazolium salt in the mitochondria, 25 displayed on the right y-axis as optical density. There is no obvious toxic effect of TS-10 on the MTS/PMS marker or on the morphology of the cells, as can be observed using a light microscope, at any concentration of TS-10/T3 used.

#### Example 5 - Comparisons of Human TR- $\alpha$ and Human TR- $\beta$

### Competition for [125I]T<sub>3</sub> binding to TR LBD by T<sub>3</sub> and Triac

The drug, Triac, is a thyroid hormone agonist. Triac is 3,5,3'-triiodothyroacetic acid and is described in Jorgensen, Thyroid Hormones and Analogs in *Hormonal Proteins and Peptides, Thyroid Hormones* at 150-151 (1978). Another

compound that can be used in place of Triac is 3,5-diiodo-3'-isopropylthyroacetic acid. Competition assays are performed to compare the displacement of [ $^{125}I$ ]T<sub>3</sub> from binding with human TR- $\alpha$  LBD or human TR- $\beta$  LBD by unlabeled T<sub>3</sub> or Triac. The results of such assays are depicted in **FIG. 16**.

Standard binding reactions are prepared containing 1 nM [<sup>125</sup>I]T<sub>3</sub>, 30 fmol of human TR-α (empty symbols) or β (solid symbols), and various concentrations of competing unlabeled T<sub>3</sub> (circles) or Triac (triangles). Assays are performed in duplicate.

# 10 Competition for [125I]T<sub>3</sub> binding to variant TR LBD by T<sub>3</sub>, Triac and GC-1

The following assays residues involved in selective binding among TR isoforms. Competition assays are performed to compare the displacement of [125]T]T<sub>3</sub> from binding with wild-type human TR-α LBD or human TR-β LBD, to a variant form of the TR LBDs by unlabeled T<sub>3</sub>, Triac or GC-1. A variant TR-α or TR-β is constructed by substituting an amino acid found in the corresponding position of the other TR isoform. For example, asparagine 331 in human TR-β corresponds to serine 277 in human TR-α. To test binding specificity contributed by this position, a variant human TR-β is constructed that contains asparagine 331 substituted with a serine residue (designated Asn331Ser or N331S). Binding assays are described in *Apriletti* 20 et al. (Protein Expression and Purification 6:363-370 (1995)). The results of such assays are depicted in FIG. 27, and summarized in Table 4 below.

Ligand	Native TR-α	Native TR-β	Mutant TR-β		
T3	20 pM	60 pM	100 pM		
T4	600	3000	ND		
Triac	20	20	100		
IpBr <sub>2</sub>	17	ND	ND		
Dimit	6000	8000	ND		

40

400

TABLE 4
Effect of TR-β Substitution N331S on Binding Affinity

Competition curves comparing wildtype TR-β versus the variant TR-β N331S for 5 binding T3, Triac or GC-1 show that the affinity of the mutant receptor for Triac was reduced to approximately the same as for T3 (vs. 3-fold greater in wild type) so that the relative affinities are similar to wild-type TR-α. The affinity for GC-1 was also reduced to several fold less than T3, as is seen with TR-α.

200

Comparison of the affinity of TR- $\beta$  variant N331S to the native TRs for 10 selected ligands is as follows:

Native TR-α for various ligands (T3, T4, Triac, IpBr2, Dimit, GC-1):

$$IpBr_2$$
. > Triac  $\cong$  T3 > GC-1 > T4 > Dimit

Native TR-β (T3, T4, Triac, Dimit, GC-1)

Triac 
$$>$$
 GC-1  $\ge$  T3  $>$  T4  $>$  Dimit

15 Variant TR-β (N331S) (T3, Triac, GC-1)

GC-1

Triac 
$$\cong$$
 T3 > GC-1.

# Scatchard Analysis of [125I]T<sub>3</sub> Binding to TR

Human TR- $\alpha$  (left panel) or human TR- $\beta$  (right panel) is assayed for T<sub>3</sub> 20 binding in the presence of increasing concentrations of [ $^{125}I$ ]T<sub>3</sub>. The apparent equilibrium dissociation constant (20 pM for I and 67 pM for  $\beta$ ) is calculated by linear regression analysis and is depicted in **FIG. 17.** 

3, 5-dibromo-4-(3',5'-diisopropyl-4'-hydroxyphenoxy) Benzoic Acid is a  $TR-\alpha$  Selective Synthetic Ligand.

3, 5-dibromo-4-(3',5'-diisopropyl-4'-hydroxyphenoxy) benzoic acid (Compound 11), the structure of which is drawn above, is assayed for binding to the two different isoforms of the TR, TR-α and TR-β. Compound 11 exhibits an IC50 of 1.6 TM for binding to TR-α and an IC50 of 0.91 TM for binding to TR-β. Assays for determining selective binding to the TR-α or TR-β LBD can include reporter assays, 15 as described herein. See also Hollenberg, *et al.*, *J. Biol. Chem.*, (1995) 270(24):14274-14280.

#### Example 6 - Preparation and Purification of a TR-α LBD

Rat TR-α LBD, residues Met122 - Val410, is purified from *E. coli* ("LBD-20 122/410"). The expression vector encoding the rat TR-α LBD is freshly transfected into *E. coli* strain BL21(DE3) and grown at 22°C in a 50-liter fermenter using 2x LB medium. At an A<sub>600</sub> of 2.5-3, IPTG is added to 0.5 mM and growth is continued for 3 h before harvesting. The bacterial pellet is quickly frozen in liquid nitrogen and stored at -70°C until processed. Extraction and purification steps are carried out at 25 4°C. The bacteria are thawed in extraction buffer (20MM Hepes, pH 8.-, 1 mM EDTA, 0.1% MTG, 0.1 mM PMSF, and 10% glycerol) at a ratio of 10 ml buffer/g bacteria. Bacteria are lysed by incubation for 15 min. with 0.2 mg/ml lysozyme and sonicated at maximum power while simultaneously homogenized with a Brinkmann homogenizer (Model PT 10/35 with generator PTA 35/2) until the solution loses its 30 viscosity. After centrifugation for 10 min at 10,000 g, the supernatant is adjusted to 0.4 M KCl, treated with 0.6% PEI to precipitate fragmented DNA, and centrifuged for 10 min at 10,000 g. The rat TR-α LBD in the supernatant is then precipitated with 50% ammonium sulfate and centrifuged for 10 min at 10,000 g. The precipitate is

resuspended with buffer B (20 mM Hepes, pH 8.0, 1 mM EDTA, 1 mM DTT, 0.1 mM PMSF, 0.01% Lubrol, and 10% glycerol) to a final conductivity of 9 mS/cm (approx. 0.7 M ammonium sulfate) and centrifuged 1 h at 100,000g. The supernatant is frozen in liquid nitrogen and stored at -70°C.

The crude extract is thawed, bound with a tracer amount of [<sup>125</sup>I]T<sub>3</sub>, and loaded directly onto a phenyl-Toyopearl hydrophobic interaction column (2.6 x 18 cm, 95 ml bed volume) at 1.5 ml/min. The column is eluted with a 2-h gradient from 0.7 ammonium sulfate, no glycerol to no salt, 20% glycerol in buffer C (20 mM Hepes, pH 8.0, 0.5 mM EDTA, 1 mM DTT, 0.2 mM PMSF). The rat TR-α LBD prebound to tracer [<sup>125</sup>I]T<sub>3</sub> (less than 0.005% of total rat TR-α LBD) is detected using a flow-through gamma emission detector, whereas unliganded rat TR-I LBD is assayed by postcolumn [<sup>125</sup>I]T<sub>3</sub> binding assays (described herein).

The phenyl-Toyopearl unliganded rat TR-α LBD peak fractions are pooled, diluted with buffer B to a conductivity of 0.5 mS/cm (equivalent to approx. 20 mM ammonium sulfate), loaded onto a TSK-DEAE anion-exchange column (2 x 15 cm, 47 ml bed volume) at 4 ml/min, and eluted with a 60-min gradient from 50 to 200 mM NaCl in buffer B.

The unliganded rat TR-α LBD peak fractions from TSK-DEAE are pooled, diluted twofold with buffer B, loaded at 0.75 ml/min on a TSK-heparin HPLC column 20 (0.8 x 7.5 cm, 3 ml bed volume), and eluted with a 50 to 400 mM NaCl gradient in buffer B.

The pool of unliganded rat TR-α LBD peak fractions from the TSK-heparin column is adjusted to 0.7 M ammonium sulfate, loaded at 0.75 ml/min on a TSK-phenyl HPLC column (0.8 x 7.5 cm, 3 ml bed volume), and eluted with a 60-min gradient from 0.7 M ammonium sulfate without glycerol to no salt with 20% glycerol in buffer C. The fractions containing unliganded rat TR-α LBD are pooled and incubated with a five fold excess of hormone for 1 h, the salt concentration is adjusted to 0.7 M ammonium sulfate, and the sample is reloaded and chromatographed on the same column as described above.

#### Example 7 - Crystallization of Liganded TR- $\alpha$ LBD

Material from a single LBD-122/410 preparation is divided into batches, and quantitatively bound with one of the following ligands: Dimit, T<sub>3</sub>, or Triac IpBr<sub>2</sub> (3,5dibromo-3'isopropylthyronine) for the final purification step.

To maintain full saturation of rat TR-α LBD with a ligand, and to prepare the complex for crystallization, the ligand-bound rat TR-α LBD is concentrated and desalted in an Amicon Centricon-10 microconcentrator (McGrath et al, *Biotechniques*, (1989) 7:246-247, incorporated by reference herein), using 10 mM Hepes (pH 7.0), 3.0 mM DTT, and 1.0 nM to 10 nM ligand.

10 Factorial crystallization screening trials (Jancarik & Kim, J. Appl. Crystallogr. (1991) 24:409-411, incorporated by reference herein) are carried out for rat TR-α LBD bound to selected ligands using hanging-drop vapor diffusion at 17°C (with 1  $\mu l$ protein solution, 1 µl precipitant solution and a 0.5 ml reservoir using silanized coverslip: (McPherson, Preparation and Analysis of Protein Crystals (1982), 15 incorporated by reference herein). Rat TR-α LBD is not stable at 4°C and is stored at -80°C, where it maintains its avidity for hormone and its crystallizability for approximately two to three months. These procedures are carried out as described in McGrath, M.E. et al., J. Mol. Biol. (1994) 237:236-239 (incorporated by reference). Crystals are obtained in condition 21 of the screening trials (Jancarik & Kim 1991) 20 and conditions are then optimized. Wedge-shaped crystals are reproducibly obtained with hanging-drop vapor fusion at 22°C with 15% 2-methyl-2,4-pentanediol (MPD), 0.2 M ammonium acetate and 0.1 M sodium cacodylate (pH 6.7), 3 mM DTT, with 2 ul protein solution, 1 ul precipitant solution and a 0.6 ml reservoir using silanized coverslip, and with 8.7 mg/ml (Dimit), 5.5 mg/ml (IpBr<sub>2</sub>), 5 mg/ml (Triac), or 2.3 25 mg/ml (T<sub>3</sub>) over a period of three days. Under these conditions, diffraction quality crystals (dimension 0.5 x 0.2 x 0.0075 mm<sup>3</sup>) can be grown at ambient temperature (22°C). The best crystals have a limiting dimension of approximately 100 Tm and are obtained at a protein concentration between 2.3 and 8.7 mg/ml in the presence of 3 mM DTT. The crystals are of the monoclinic space group C2, with one monomer in 30 the asymmetric unit.

# Example 8 - Crystallization of Human TR- $\beta$ LBD Complexed with T3, Triac, or GC-1

Human TR- $\beta$  LBD complexed with T<sub>3</sub>, Triac, or GC-1 are purified according to the same procedures described above for the rat TR- $\alpha$  LBD, with the following 5 modifications.

The expression of human TR-β LBD differs from the rat TR-α LBD in that the human TR-β LBD residues extend from the amino acid at position 716 through the amino acid at position 1022, according to the amino acid numbering scheme for the various nuclear receptor LBDs depicted in **FIG. 3. FIG. 3** illustrates a numbering scheme applicable to all of the nuclear receptors listed as well as to any additional homologous nuclear receptors. The vertical lines on **FIG. 3** at position 725 and at position 1025 delineate the preferred minimum amino acid sequence necessary to obtain adequate binding of ligand. The amino acid sequence from position 716 to position 1022 according to the numbering scheme of **FIG. 3** corresponds to the amino acid positions 202 to 461 according to the conventional numbering of the amino acid sequence of human TR-β which is publicly available. Also, the human TR-β LBD is expressed with a histidine tag, as described in Crowe *et al.*, *Methods in Molecular Biology* (1994) *31*:371-387, incorporated by reference herein.

The purification of human TR-β LBD is the same as that described above for the rat TR-α LBD with the following exceptions. First, before the purification step using the hydrophobic interaction column, a step is added in which the expressed human TR-β LBD is purified using a nickel NTA column (commercially available from Qiagen, Chatsworth, CA) according to manufacturer's instructions, and eluted with 200 mM imidazole. The second difference is that in the purification of the human TR-β LBD, the purification step using a heparin column is omitted.

The crystallization of human TR-β LBD bound to T<sub>3</sub>, Triac or GC-1 is as follows. Crystals are obtained in condition 7 of the factorial screen using hanging drops as before at ambient temperature (22°C) using the factorial crystallization screening trials of Jancarik & Kim (1991) and using the commercially available 30 product from Hampton Research, Riverside). The following are optimum conditions: hexagonal bipyrimidal crystals are grown at 4°C for 2-3 days from hanging drops containing 1.0-1.2 M sodium acetate (pH unadjusted) and 0.1 M sodium cacodylate (pH 7.4), 3 mM DTT, with either a 1 μl protein solution, 1 μl precipitant solution or 2

µl protein solution. 1 µl precipitant solution and a 0.6 ml reservoir using silanized coverslip, at a protein concentration of 7-10 mg/ml. The best crystals have a limiting dimension of 200 μm. The following are optimum conditions for crystallization of the TR-β LBD with GC-1: hexagonal bipyrimidal crystals are grown at 4°C for 2-3 days from hanging drops containing 0.8-1.0M sodium acetate (pH unadjusted), 50-200nM sodium succinate, and 0.1M sodium cacodylate (pH 7.2), 3mM DTT, 1 μl protein solution, 1 μl precipitant solution and a 0.6ml reservoir using silanized coverslip, at a protein concentration of 7-10 mg/ml. The best crystals have a limiting dimension of 200μM. The unit cell dimensions are cell length a=b=68.73, cell length 10 c=130.09. The unit cell angles are α=90°, β=90°, γ=120°.

The crystal system for human TR- $\beta$  LBD bound to T<sub>3</sub>, Triac or GC-1 is trigonal with the space group p3<sub>1</sub>21. The unit cell dimensions are cell length a = cell length b = 68.448 angstroms, cell length c = 130.559 angstroms. The angles are  $\alpha$  = 90°,  $\beta$  = 90°, gamma = 120°.

15

# Example 9 - Determination of Liganded TR- $\alpha$ LBD and TR- $\beta$ Crystal Structures

Data from each cocrystal (Rat TR-α LBD with Dimit, T3 and IpBr2; Human TR-β LBD with Triac and GC-1) is measured on a Mar area detector at Stanford 20 Synchrotron Radiation Laboratory beamline 7-1 (λ = 1.08 angstroms) using 1.2° oscillations. Data from the cocrystal of the hTR-β LBD with Triac is measured on a Mar area detector at Stanford Synchrotron Radiations Laboratory beamline 7-1 (λ = 1.08 angstroms) using 1.0 oscillations. Data from the cocrystal of the hTR-β LBd with GC-1 is measured on a R-axis II area detector on a Rigaku rotating Cu anode 25 (50kV, 300mA). The crystals are transferred into a cryosolvent containing 1.2M sodium acetate, 0.1M sodium cacodylate, adn 15% glycerol followed by a second transfer into 30% glycerol, then flash frozen in liquid nitrogen. An orientation matrix for each crystal is obtained using DENZO. The reflections are integrated with DENZO (commercially available from Molecular Structure Corp., The Woodlands, 30 Texas) and are scaled with SCALEPACK (as described in Otwinowski, Z, *Proceedings of the CCP4 Study Weekend: "Data Collection and Processing,"* 56-62 (SERC Daresbury Laboratory, Warrington, UK 1993) incorporated by reference).

For rTR-α cocrystals, data from the T<sub>3</sub> cocrystal is measured with the b\* axis approximately parallel with the spindle. The crystals are flash frozen at -178°C in a nitrogen gas stream with the MPD mother liquor serving as the cryosolvent. An orientation matrix for each crystal is determined using REFIX (Kabsch, W., *J. Appl. Crystallogr.* (1993) 26:795-800 incorporated by reference). Reflections are integrated with DENZO, and are scaled with SCALEPACK.

For the T<sub>3</sub> data set, Bijvoet pairs are kept separate, and are locally scaled using MADSYS (W. Hendrickson (Columbia University) and W. Weis (Stanford University)).

10 Cocrystals prepared from the three isosteric ligands are isomorphous. MIR analysis is performed using programs from the CCP4 suite (Collaborative Computational Project, N.R. Acta Crystallogr. (1994) D50:760-763, incorporated by reference herein). Difference Pattersons is calculated for both T<sub>3</sub> and IpBr<sub>2</sub>, taking the Dimit cocrystal as the parent. The positions of the three iodine atoms in the T<sub>3</sub> 15 difference Patterson are unambiguously determined from the Harker section of the density map as peaks of 11[ above background. The positions for the two bromine atoms in the IpBr<sub>2</sub> cocrystals, are located independently, as peaks 8[ above the noise level. Phases for the LBD-122/410 are calculated from the solution to the IpBr<sub>2</sub> difference Patterson, and are used to confirm the location of the unique third iodine of 20 the T<sub>3</sub> cocrystal. Halogen positions are refined with MLPHARE, including the anomalous contributions from the iodine atoms (Otwinowski, Z, Proceedings of the CCPR Study Weekend 80-86 (SERC Daresbury Laboratory, Warrington, UK 1991)). The MIRAS phases are improved through solvent flattening/histogram matching using DM (Cowtan, K., Joint CCP4 and ESF-EACBM Newsletter on Protein 25 Crystallography (1994) 31: 34-38, incorporated by reference herein).

A model of the LBD-122/410 with Dimit bound is built with the program O from the solvent flattened MIRAS 2.5 angstrom electron density map (Jones *et al.*, *Acta Crystallogr*. (1991) A 47:110-119, incorporated by reference herein). The initial model, without ligand, (Rcryst = 40.1%), is refined using least-squares protocols with XPLOR. The Dimit ligand is built into unambiguous Fo-Fc difference density during the following round. Subsequent refinement employs both least-squares and simulated annealing protocols with XPLOR (Brunger *et al.*, *Science* (1987) 235:458-460), incorporated by reference herein). Individual atomic B-factors are refined

isotropically. As defined in PROCHECK, all residues are in allowed main-chain torsion angle regions as described in Laskowski *et al.*, *J. Appl. Crystallogr.*, (1993) 26:283-291, incorporated by reference herein. The current model is missing 34 residues (Met<sub>122</sub>-Gln<sub>156</sub>) at the N-terminus, and 5 residues (Glu<sub>406</sub>-Val<sub>410</sub>) at the C-5 terminus.

In addition, the following residues are not modeled beyond Cβ due to poor density: 184, 186, 190, 198, 206, 209, 240, 301, 330, 337, 340, 343, 359, and 395. The average B-value for protein atoms is 34.5 Å<sup>2</sup>. The final model consists of the LBD-122/410, residues Arg<sub>157</sub>-Ser<sub>183</sub>, Trp<sub>185</sub>-Gly<sub>197</sub>, Ser<sub>199</sub>-Asp<sub>206</sub> and Asp<sub>208</sub>-Phe<sub>405</sub>; 10 three cacodylate-modified cysteines: Cys<sub>334</sub>, Cys<sub>380</sub> and Cys<sub>392</sub>; and 73 solvent molecules modeled as water (2003 atoms).

\*
$$R_{sym} = 100 \times \Sigma_{hkl} \Sigma_i \mid I_i - I \mid / \Sigma_{hkl} \Sigma_i I_i$$
  
† $R_{der} = 100 \times \Sigma_{hkl} \mid F_{PH} - F_H \mid / \Sigma_{hkl} \mid F_P \mid$ 

The occupancy for the two bromine sites is set to 35 electrons. The occupancies of the 15 iodine sites are relative to this value.

§Phasing power =  $\langle FH \rangle$ ,  $/\langle \epsilon \rangle$ , where  $\langle FH \rangle$  is the mean calculated heavy atom structure factor amplitude and  $\langle \epsilon \rangle$  is the mean estimated lack of closure.

4Rcullis =  $\langle \in \rangle / \langle iso \rangle$ , where  $\langle \in \rangle$  is the mean estimated lack of closure and  $\langle iso \rangle$  is the isomorphous difference.

20 ¶Reryst = 100 x  $\Sigma_{hkl}$  | F<sub>o</sub>-Fe| /  $\Sigma_{hkl}$  | F<sub>o</sub>| where F<sub>o</sub> and F<sub>c</sub> are the observed and calculated structure factor amplitudes (for data F/ $\sigma$  > 2). The Rfree was calculated using 3% of the data, chosen randomly, and omitted from the refinement.

§ Correlation coefficient = 
$$\Sigma_{hkl}$$
 ( $|F_o| - |F_o|$ ) x ( $|F_c| - |F_c|$ )/ $\Sigma_{hkl}$  ( $|F_o| - |F_o|$ )<sup>2</sup>x $\Sigma_{hkl}$  ( $|F_c| - |F_c|$ )<sup>2</sup>

25

# Example 10. Phasing of the rTR- $\alpha$ LBD and hTR- $\beta$ LBD complex with Triac

Due to the possible non-isomorphism of the rTRα LBD complex with Triac, a molecular replacement solution is determined using AMORE (Navaza, J., Acta 30 Crystallographica Section A-Fundamentals of Crystallography (1994) 50:157-63 from a starting model consisting of rTRI LBD complex with T<sub>3</sub>, but with the ligand, all water molecules, and the following residues omitted: Asn 179, Arg228, Arg262, Arg266, and Ser 277. Strong peaks are obtained in both the rotation and translation

searches, with no significant (> 0.5 times the top peak) false solutions observed (Table 6). Strong positive density present in both the anomalous and conventional difference Fourier maps confirm the solution. Maps are calculated using sigma-A weighted coefficients output by REFMAC (Murshudov, et al. "Application of 5 Maximum Likelihood Refinements," in Refinement of Protein Structures, Proceedings of Daresbury Study Weekend (1996)) after 15 cycles of maximum likelihood refinement. Triac, the omitted residues, and water molecules 503, 504, 534 (following the numbering convention for the TR complex with T3) are built into the resulting difference density using O (Jones et. al.); the conformations of these residues are further confirmed in a simulated-annealing omit map (Brunger et. al.). The complete model is then refined using positional least-squares, simulated annealing, and restrained, grouped B factor refinement in XPLOR to an Reryst of 23.6% and an Rfree of 24.1%

Phasing of a related LBD using the structure of the rTR-α LBD is conducted 15 as follows. A molecular replacement solution for the hTR-β LBD complex with Triac is determined using AMORE from a starting model consisting of the rTR-α LBD complexed with T3, but with the ligand and all water molecules omitted. Strong peaks are obtained in both the rotation and translation searches, with no significant (>0.5 times the top peak) false solutions (Table 7). Strong positive density present in 20 both the anomalous and conventional difference Fourier maps confirm the solution. Initial maps are calulated using sigma-A weighted coefficients output by REFMAC after 9 cycles of maximum likelihood refinement. The real-space fit for each residues was calculated using OOPS (Kleywegt, GJ and Jones, TA, OOPS-a-daisy, ESF/CCP4 Newsletter 30, June 1994, pp. 20-24) and the residues with a real-space fit less than 2 25 standard deviations below the mean removed: Ala253-Lys263; Glu245-Leu250. To reduce bias, the following residues were modeled as alanine: Arg282, Arg316, Arg 320, Asn 331. Cycles of rebuilding and positional least-squares, simulated annealing, and restrained, grouped B factor refinement with XPLOR produce a model with an  $R_{cryst}$  of 25.3 and an  $R_{free}$  of 28.9%. The final model consists of hTR- $\beta$  LBD residues 30 Glu202-Gln252, Val264-Glu460; three cacodylate-modified cysteines with the cacodylate moeity modeled as free arsenic: Cys294, Cys298, Cys388, and Cys434; and 35 solvent molecules modeled as water.

# EXAMPLE 11. CONNECTING QSAR WITH STRUCTURE IN THE THYROID HORMONE RECEPTOR

The conclusions of classic thyroid hormone receptor quantitative structureactivity relationships may be summarized as follows:

5 1) the  $R_4$ '-hydroxyl group functions as a hydrogen bond donor;

2) the amino-propionic acid interacts electrostatically through the carboxylate anion with a positively charged residue from the receptor;

3) the preferences of  $R_3/R_5$  substituent are I>Br>Me>>H;

4) the preferences of the  $R_3$ '-substituent are Ipr>I>Br>Me>>H.

10 The structure of the thyroid hormone receptor ligand binding domain complexed with the agonists T3, IpBr<sub>2</sub>, Dimit, Triac, and GC1 as provided herein, permits:

 the identification of receptor determinants of binding at the level of the hydrogen bond;

2) the association of these determinants with the predictions of classic thyroid hormone receptor QSAR; and

3) prediction as to which determinants of binding are rigid, and which are flexible, for both the ligand and the receptor.

This classification for the agonists of the type ( $R_1$ =amino-propionic, acetic acid;  $R_3,R_5$ =I,Br,Me;  $R_3$ '=Ipr,I) is given below (for the representative ligand  $T_3$ );

20

15

F = Fiducial (always satisfied)

A = Adjustable

30

Based upon the methods and data described herein, the following is an embodiment of the computational methods of the invention, which permit design of nuclear receptor ligands based upon interactions between the structure of the amino acid residues of the receptor LBD and the four different ligands described herein. The

small molecule structures for the ligands can be obtained from Cambridge Structural Database (CSD), and three dimensional models can be constructed using the methods described throughout the specification. The following are factors to consider in designing synthetic ligands:

- 1) Histidine 381 acts as a hydrogen bond acceptor for the R<sub>4</sub>' hydroxyl, with the optimal tautomer maintained by water molecules. See **FIG. 23 and FIG 24.** Histidine is the only hydrophilic residue in this hydrophobic pocket that surrounds the R<sub>4</sub>' substituent. Histidine can be either a hydrogen bond acceptor or donor, depending on its tautomeric state. It is preferably a hydrogen bond donor, but can tolerate being a hydrogen bond acceptor, as for example, when there is a methoxy at the R<sub>4</sub>' position of the ligand;
  - 2) Arginines 228, 262, and 266 interact directly and through water-mediated hydrogen bonds with the  $R_1$ -substituent, with the electrostatic interaction provided by Arginine 266 (as in the Triac complex). This polar pocket is illustrated by **FIG. 23** -
- 15 **FIG. 25**. **FIG. 23** depicts T<sub>3</sub> in the TRI ligand binding cavity, where T3's aminopropionic R<sub>1</sub>- substituent interacts with Arg 228, HOH502, H9H503 and HOH504 via hydrogen bonds. **FIG. 24** depicts Triac in the ligand binding cavity, with its -COOH R<sub>1</sub> substituent in the polar pocket. In **FIG. 24**, Arg 228 no longer shares a hydrogen bond with the ligand, but the -COOH R<sub>1</sub> substituent forms hydrogen bonds with Arg
- 20 266. **FIG. 25** superimposes T<sub>3</sub> and Triac in the ligand binding cavity and shows several positionally unchanged amino acids and water molecules, and selected changed interacting amino acids and water molecules. The three figures illustrate parts of the polar pocket that can change and those parts that do not move upon binding of different ligands. For example, the Arg 262 at the top of the polar pocket
- 25 does not move, even when the R<sub>1</sub> substituent has changed from a -COOH to an aminopropionic acid group. However, the other two Arginines, Arg 228 and Arg 266, demonstrate flexibility in the polar pocket to respond to the change in the size or chemical naure of the R<sub>1</sub> substituent.
- 3) Inner and outer pockets for the R<sub>3</sub>/R<sub>5</sub> substituents are formed by 30 Ser260, Ala263, Ile299; and Phe 218, Ile221, Ile222, respectively. See **FIGS. 21 and 22.** The inner pocket is filled by either the R<sub>3</sub> or the R<sub>5</sub> substituent, regardless of the size of the substituent, and may act as a binding determinant by positioning the ligand in the receptor. Optimally, the inner pocket amino acids interact with an R<sub>3</sub> or R<sub>5</sub>

substituent that is no larger than an iodo group. If the inner pocket is filled by the R<sub>3</sub> substituent, then the outer pocket interacts with the R<sub>5</sub> substituent and vice versa. The outer pocket can adjust to the size of its substituent through main chain motion centered at the break in helix 3 (Lys220-Ile221), suggesting that the bending of H3, and motion of the N-terminal portion of H3, may represent a conformational change induced on ligand binding. The outer pocket has greater flexibility than does the inner pocket in terms of accommodating a larger substituent group.

4) A pocket for the R<sub>3</sub>'-substituent is formed by Phe 215, Gly290, Met388. The pocket is incompletely filled by the R<sub>3</sub>'-iodo substituent, and 10 accommodates the slightly larger 3'-isopropyl substituent by movement of the flexible Met388 side chain and the H7/H8 loop. This pocket can accommodate R<sub>3</sub>' substituents that are even larger than isopropyl, for example, a phenyl group.

The above information will facilitate the design of high affinity agonists and antagonists by improving automated QSAR methodologies and informing manual modeling of pharmaceutical lead compounds. For example, the inclusion of discrete water molecules provides a complete description of hydrogen bonding in the polar pocket for use with pharmacophore development: also, the identification of mobile and immobile residues within the receptor suggests physically reasonable constraints for use in molecular mechanics/dynamics calculations.

20

#### EXAMPLE 12. DESIGN OF AN INCREASED AFFINITY LIGAND

Direct interaction between the receptor and the ligand is limited in the polar pocket, which interacts with the R<sub>1</sub> substituent. While the lack of complementarity may contain implications for biological regulation, it also provides an opportunity for 25 increasing affinity by optimizing the interaction between the amino acids of the polar pocket and the R<sub>1</sub> substituent of a synthetic ligand. The structure of the receptor-ligand interactions described herein enables design of an increased affinity synthetic ligand having two complementary modifications:

1) Remove the positively charged amine. The strongly positive 30 electrostatic potential predicted for the polar pocket suggests that the positively charged amine of the aminopropionic acid R<sub>1</sub> substituent may be detrimental to binding. Suitable groups for substitution are suggested by the nature of nearby hydrogen bond partners: for example, Thr 275 O or Ser 277 N. See e.g. Tables in Appendix 2. For example, any any negatively charged substituent would be

compatible for interacting with the amino acids of the polar pocket, including carboxylates, carbonyl, phosphonates, and sulfates, comprising 0 to 4 carbons. Another example of an  $R_1$  substitution is an oxamic acid that replaces the amine of the naturally occurring ligand with one or more carbonyl groups.

Incorporate hydrogen bond acceptor and donor groups into the R<sub>1</sub>-5 2) substituent to provide broader interactions with the polar pocket scaffold. Such hydrogen bond acceptor and donor groups incorporated into the R1-substituent will allow interactions that would otherwise occur with water molecules in the polar pocket. Specific waters include HOH 504 (hydrogen bonds with Ala 225 O and Arg 10 262 NH); and HOH 503 hydrogen bonds with Asn 179 OD1, Ala 180 N), both of which are present in all four complexes (TR LBD complexed with T3, TR LBD complexed with IpBr2, TR LBD complexed with Dimit and TR LBD complexed with Triac). Analysis of the hydrogen bonding network in the polar pocket suggests replacement of HOH 504 with a hydrogen bond acceptor, and HOH 503 with an 15 hydrogen bond donor (although the chemical nature of asparagine probably permits flexibility at this site). Thus, incorporating a hydrogen bond acceptor in an R1 substituent that could take the place of the HOH504 or incorporating a hydrogen bond acceptor in an R1 substituent that could positionally replace the HOH503, or a combination thereof, are methods of designing novel synthetic TR ligands.

These two design approaches can be used separately or in combination to design synthetic ligands, including those in Table 5 (below).

A corollary to this approach is to design specific interactions to the residues Arg262 and Asn 179. The goal is to build in interactions to these residues by designing ligands that have R<sub>1</sub> substituents that form hydrogen bonds with water 25 molecules or charged residues in the polar pocket.

High-affinity ligands also may be designed and selected using small molecules that bind to proximal subsites of the target nuclear hormone receptor that are identified in a structure-based screen and then linked together in their experimentally determined bound orientiations. Such a method has been described in design of high-30 affinity ligands for the FK506 binding protein (FKBP), stromelysin, gelatinase A, and human papillomavirus E2 (Hajduk *et al.*, *Science 278*:497-499 (1997)), which reference and its references are incorporated herein by reference. The preferred small molecules for screening are compounds of Formula I or derivatives thereof. For

example, a compound of Formula I (φ-X-φ) or a derivative thereof (φ-X or X-φ) is screened for binding a target nuclear hormone receptor LBD. Proximal subsites of the nuclear hormone receptor include the hydrophobic and polar pockets of the LBD, and substites extended therefrom. As an example, Fourier transformation or nuclear 5 magnetic resonance (NMR) -based structure screens can be used. When a NMR-based screen is used, binding can be detected from the amide chemical shift changes observed in two-dimensional heteronuclear single quantum correlation (HSQC) spectra aquired in the presence and absence of added compound. Once two ligands are identified that bind to the receptor, the crystal or solution structure of the ternary 10 complex is determined. From the structural information, a compound is synthesized which links the two ligands, where the linker is selected based on structural information. The new compound is then screened for binding affinity, for example, using a binding assay as described herein. Only a few linked ligands need to synthesized and screened when using this approach.

15 Compounds of the invention also may be interatively designed from structural information of the compounds described above using other structure-based design/modeling techniques (Jackson, R.C., Contributions of protein structure-based drug design to cancer chemotherapy. Semninars in Oncology, 1997, 24(2)L164-172; and Jones, T.R., et al., J. Med. Chem., 1996 39(4):904-917).

Table 5: Synthetic TR Ligands

5

R1	R2	R3	R5	R6	X	R'2	R'3	R'4	R'5	R'6
СО2Н	Н	Me	Me	Н	О	Н	Me	ОН	Me	Н
CH2CO2H		I	I		S		Et	SH	Et	
СН2СН2СО2Н		Br	Br				nPr	NH2	nPr	
CH2CH(NH2)CO2H		CI	Cl				iPr		iPr	
ОСН2СО2Н		Et	Et				Ph		nBu	
осн2сн2со2н		ОН	ОН				I		nPen	
NHCH2CO2H		NH2	NH2				Br	·	nHex	
NHCH2CH2CO2H		SH	SH				Cl		Ph	
CH2COCOCO2H									hetero	
•									cycle	
NHCOCOCO2H									aryl	
СОСО2Н										
CF2CO2H										
СОСН2СО2Н										

Any combination of the above substituents in the biphenyl ether scaffold structure shown above may result in a potentially pharmacologically useful ligand for the 10 thyroid hormone receptor. These novel ligands may be antagonists of the thyroid receptor.

**TABLE 6: TR-α LBD-122/410** 

	IADI	LE G. IN-G LD	D-122/710	
	Dimit	Т3	$IpBr_2$	Triac
Data collection				
Cell dimensions	•			
a (Å)	117.16	117.19	117.18	118.19
b (Å)	80.52	80.20	80.12	81.37
c (Å)	63.21	63.23	63.13	63.73
β (°)	120.58	120.60	120.69	121.00
Resolution (Å)	2.2	2.0	2.1	2.45
Obs. Reflections, (no.)	57031	64424	66877	83573
Unique Reflections, (no.)	22327	21023	23966	18453
Completeness, (%)	87.0	82.4	93.7	96.0
*R <sub>sym</sub> (%)	3.9	3.5	4.5	7.5
Phasing (15.0 - 2.5Å)				
†R <sub>der</sub> (%)	- -	19.6	11.6	
No. of sites	-	3	2	
‡Occupancy	-	44.6 (19.8)	35.0	
(Anomalous)	-	50.2 (23.7)	35.0	
		39.2 (22.3)		
§F <sub>H</sub> /E				
centric (acentric)		•		
15.0-5.0 Å	-	3.67 (4.61)	2.25 (3.09)	
5.0 <b>-3</b> .0 Å	-	2.23 (2.75)	1.25 (1.85)	
3.0 <b>-2</b> .5 Å	•	1.64 (1.99)	1.15 (1.57)	
$\P R_{Cullis}(\%)$				
15.0-5.0 Å	-	33	44	
5.0-3.0 Å	-	45	63	
3.0-2.5 Å	-	60	65	
Mean figure of merit MR Phasing (10-3.5Å)	0.62	-	-	
Rotation Search:	-			$\Theta_1 = 309.37$
Euler Angles (°)				$\Theta_2 = 48.96$
Edici Migics ( )				$\Theta_3 = 127.28$
				03 - 127.28
§ correlation coefficient				34.3
Translation Search: Fractional coordinates				x = 0.1571
				y = 0.000
				z = 0.3421
§ correlation Coefficient				65.8
'R factor				31.2
11 140 000				

Refinement Resolution (Å)	15.0-2.2	5.0 - 2.0	15.0 - 2.2	25-2.5
¶R <sub>cryst (%)</sub>	20.5	22.1	21.4	23.6
R <sub>free (%)</sub>	22.7	24.0	22.4	24.1

**TABLE 7: TR-β LBD-202/461** 

	Triac	Т3	GC1
Data collection			
Space Group	<del></del>	P3121	
Cell dimensions			
a (Å)	68.9	68.45	68.73
c (Å)	131.5	130.56	130.09
Resolution (Å)	2.4	3.1	2.8
Obs. Reflections, (no.)	80196	55103	54104
Unique Reflections. (no.)	14277	6847	8987
Coverage (%)	97.0	95.7	97.1
*R <sub>sym</sub> (%)	5.1	4.6	5.5
MR Phasing (15.0 - 3.5Å)			
Rotation Search	$\Theta_1 = 39.13$		
Euler Angles (°)	Θ <sub>2</sub> =68.00		
	$\Theta_3 = 323.6$		
§ correlation coefficient	21.6		
(Highest false peak)	(10.8)		
Translation Search	x=0.748		
Fractional Coordinates	y=0.158		
	z=0.167		
§ correlation coefficient	57.5		
(Highest false peak)	(38.7)		
	0.612		
*R factor	40.7	40.8	
Refinement			
Resolution (Å)	30-2.4		30-2.9
¶R <sub>cryst (%)</sub>	25.3		27.3
R <sub>free (%)</sub>	28.9		33.4

All publications and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication or patent application was specifically and individually indicated to be incorporated by reference. The nuclear receptor ligands, particularly the TR ligands, of these

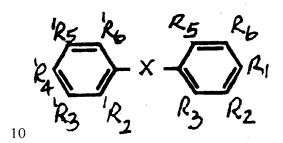
references are herein incorporated by reference and can be optionally excluded from the claimed compounds with a proviso.

Headings and subheadings are presented only for the convenience of the reader and should not be used to construe the meaning of terms used within such 5 headings and subheadings.

The invention now being fully described, it will be apparent to one of ordinary skill in the art that many changes and modifications can be made thereto without departing from the spirit or scope of the appended claims.

#### WHAT IS CLAIMED IS:

1. A method of modulating the activity of a thyroid hormone receptor (TR) which comprises administering to a mammal in need thereof a compound of the 5 formula:



wherein said compound fits spatially and preferentially into a TR ligand binding domain (TR LBD) and comprises the following substituents:

- (i) an R<sub>1</sub>-substituent comprising an anionic group that interacts with a side chain nitrogen atom of an arginine corresponding to a residue selected from the group consisting of Arg228, Arg262, and Arg266 of human TR-α, and Arg282, Arg316 and Arg320 of human TR-β, and wherein the anionic group is 1.7-4.0Å from the nitrogen atom;
- (ii) an R<sub>2</sub>-substituent comprising a hydrophobic or hydrophilic group that 20 fits spacially into the TR LBD;
- (iii) an R<sub>3</sub>-substituent comprising a hydrophobic or hydrophilic group that interacts with a side chain atom of a serine, alanine or isoleucine corresponding to a residue selected from the group consisting of Ser260, Ala263 and Ile299 of human TR-α, and Ser314, Ala317 and Ile352 of human TR-β, and wherein the hydrophobic or hydrophilic group is 1.7-4.0Å from the side chain atom;

(iv) an R<sub>5</sub>-substituent comprising a hydrophobic or hydrophilic group that interacts with a side chain atom of a phenylalanine or isoleucine corresponding to a residue selected from the group consisiting of Phe218, Ile221 and Ile222 of human TR-I, and Phe272, Ile275 and Ile276 of human TR-β, and wherein the hydrophobic or 5 hydrophilic group is 1.7-4.0Å from the side chain atom;

- (v) an R<sub>6</sub>-substituent comprising a hydrophobic or hydrophilic group that fits spacially into the TR LBD;
- (vi) an X-substituent comprising a hydrophobic or hydrophilic group that interacts with a side chain atom of a leucine corresponding to a residue selected from
   the group consisting of Leu276 and Leu292 of human TR-α, and Leu 330 and Leu346 of human TR-β, and wherein the hydrophobic or hydrophilic group is 1.7-4.0Å from the side chain atom;
  - (vii) an R<sub>2</sub>'-substituent comprising a hydrophobic or hydrophilic group that fits spacially into the TR LBD;
- 15 (viii) an R<sub>3</sub>'-substituent comprising a hydrophobic group that interacts with a side chain atom of a phenylalamine, glycine or methionine corresponding to a residue selected from the group consisting of Phe215, Gly290, and Met388 of human TR-α, and Phe269, Gly344, Met442 of human TR-β, and wherein the hydrophobic group is 1.7-4.0Å from the side chain atom;
- 20 (ix) an R<sub>4</sub>'-substituent comprising an hydrogen bond donor or acceptor group that interacts with a side chain carbon or nitrogen atom of a histadine corresponding to residue His381 of human TR-α, and His435 of human TR-β, and wherein the hydrogen bond donor or acceptor group is 1.7-4.0Å from the side chain atom;

(x) an R<sub>5</sub>'-substituent comprising a hydrophobic or hydrophilic group that fits spacially into the TR LBD;

- (xi) and R<sub>6</sub>'-substituent comprising a hydrophobic or hydrophilic group that fits spacially into the TR LBD;
- wherein said compound is other than a thyronine or thyronine-like compound disclosed in a reference cited in Appendix I, and wherein the activity of said TR is modulated.
  - 2. The method according to claim 1,
- 10 wherein R<sub>1</sub> is
  - -O-CH<sub>2</sub>CO<sub>2</sub>H, -NHCH<sub>2</sub>CO<sub>2</sub>H,
  - -CO<sub>2</sub>H, -CH<sub>2</sub>CO<sub>2</sub>H, -CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>H, -CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>H,
  - $-CH_2CH(NH_2)CO_2H$ ,

-CH<sub>2</sub>CH[NHCOCH $\phi_2$ ]CO<sub>2</sub>H,

- -CH<sub>2</sub>CH[NHCO(CH<sub>2</sub>)<sub>15</sub>CH<sub>3</sub>
- $1CO_2H$ ,
- -CH<sub>2</sub>CH[NH-FMOC]CO<sub>2</sub>H,
- -CH<sub>2</sub>CH[NH-tBOC]CO<sub>2</sub>H, or a carboxylate connected to the ring with a 0 to 3 carbon linker,
- -PO<sub>3</sub>H<sub>2</sub>, -CH<sub>2</sub>PO<sub>3</sub>H<sub>2</sub>, -CH<sub>2</sub>CH<sub>2</sub>PO<sub>3</sub>H<sub>2</sub>, -CH<sub>2</sub>CHNH<sub>2</sub>PO<sub>3</sub>H<sub>2</sub>, -CH<sub>2</sub>CH[NHCOCH $\phi_2$ ]PO<sub>3</sub>H<sub>2</sub>, -CH<sub>2</sub>CH[NHCO(CH<sub>2</sub>)<sub>15</sub>CH<sub>3</sub>]PO<sub>3</sub>H<sub>2</sub>,
- -CH<sub>2</sub>CH[NH-FMOC]PO<sub>3</sub>H<sub>2</sub>, -CH<sub>2</sub> CH[NH-tBOC]PO<sub>3</sub>H<sub>2</sub>, or a phosphate or phosphonate connected to the ring with a 0 to 3 carbon linker,
  - -SO<sub>3</sub>H, -CH<sub>2</sub>SO<sub>3</sub>H, -CH<sub>2</sub>CH<sub>2</sub>SO<sub>3</sub>H, -CH<sub>2</sub>CH[NHCOCH $\phi_2$ ]SO<sub>3</sub>H, -CH<sub>2</sub>CH[NHCO(CH<sub>2</sub>)<sub>15</sub>CH<sub>3</sub>]SO<sub>3</sub>H,

-CH<sub>2</sub>CH[NH-FMOC]SO<sub>3</sub>H, -CH<sub>2</sub> CH[NH-tBOC]SO<sub>3</sub>H, or a sulfate or sulfite connected to the ring with a 0 to 3 carbon linker,

or acts as the functional equivalent of CH<sub>2</sub>CH(NH<sub>2</sub>)CO<sub>2</sub>H of T3 in the molecular recognition domain when bound to a TR, wherein said R<sub>1</sub> can be optionally substituted with an amine,

# wherein R2 is

5

H, halogen, CF<sub>3</sub>, OH, NH<sub>2</sub>, SH, CH<sub>3</sub>, -Et,

or acts as the functional equivalent of H in the molecular recognition domain when bound to a TR,

### wherein R<sub>3</sub> is

-H, halogen, -CF<sub>3</sub>, -OH, -NH<sub>2</sub>, -N<sub>3</sub>, -SH, -CH<sub>3</sub>, -Et,

or acts as the functional equivalent of I in the molecular recognition domain when bound to a TR,

# wherein R5 is

-H, halogen, -CF<sub>3</sub>, -OH, -NH<sub>2</sub>, -N<sub>3</sub>, -SH, -CH<sub>3</sub>, -Et, or acts as the functional equivalent of I in the molecular recognition domain when bound to a TR, and R<sub>3</sub> can be identical to R<sub>5</sub>,

### wherein R<sub>6</sub> is

-H, halogen, -CF<sub>3</sub>, -OH, -NH<sub>2</sub>, -SH, -CH<sub>3</sub>, or acts as the functional equivalent of H in the molecular recognition domain when bound to a TR, and  $R_2$  can be identical to  $R_6$ ,

### 5 wherein R<sub>2</sub>' is

-H, halogen, -CF<sub>3</sub>, -OH, -NH<sub>2</sub>, -N<sub>3</sub>, -SH, -CH<sub>3</sub>, -Et, or acts as the functional equivalent of H in the molecular recognition domain when bound to a TR,

wherein R<sub>3</sub>' is any hydrophobic group, including

halogen, -CF<sub>3</sub>, -SH, alkyl, aryl, 5- or 6-membered heterocyclie, cyano, or acts as the functional equivalent of I in the molecular recognition domain when bound to a TR,

#### wherein R<sub>4</sub>' is

-H, halogen, -CF<sub>3</sub>, -OH, -NH<sub>2</sub>, NH<sub>3</sub>, -N(CH<sub>3</sub>)<sub>3</sub>, carboxylate, phosphonate, phosphate or sulfate, -SH, -CH<sub>3</sub>, -Et, or akyl, aryl or 5- or 6-membered heterocyclic aromatic attached through urea or carbamate linkages to O or N or S at the R<sub>4</sub>' position, or acts as the functional equivalent of OH in the molecular recognition domain when bound to a TR,

20

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### wherein R<sub>5</sub>' is

-H, -OH, -NH<sub>2</sub>, -N(CH<sub>3</sub>)<sub>2</sub> -SH -NH<sub>3</sub>, -N(CH<sub>3</sub>)<sub>3</sub>, carboxylate, phosphonate, phosphate, sulfate, branched or straight chain alkyl having 1 to 9 carbons, substituted or unsubstituted aryl, wherein said substituted aryl is substituted with halogen or 1 to 5 carbon alkyl and wherein said aryl is optionally

connected to the ring by a -CH<sub>2</sub>-, aromatic heterocycle having 5 to 6 atoms, wherein said heterocycle may be substituted with one or more groups selected from -OH, -NH<sub>2</sub>, -SH, -NH<sub>3</sub>, -N(CH<sub>3</sub>)<sub>3</sub>, carboxylate, phosphonate, phosphate or sulfate, heteroalkyl, arylalkyl, heteroaryl alkyl, polyaromatic, or polyheteroaromatic, wherein said R<sub>5</sub>' may be substituted with polar or charged groups,

wherein R<sub>6</sub>' is

-H, halogen, -CF<sub>3</sub>, -OH, -NH<sub>2</sub>, -SH, -CH<sub>3</sub>, -Et, or acts as the functional equivalent of H in the molecular recognition domain when bound to a TR,

wherein X is

O, S, SO<sub>2</sub>, NH, NR<sub>7</sub>, CH<sub>2</sub>, CHR<sub>7</sub>, CR<sub>7</sub>R<sub>7</sub>, wherein R<sub>7</sub> is alkyl, aryl or 5- or 6-membered heterocyclic aromatic,

15

5

and wherein said TR LBD ligand has an apparent Kd for binding TR LBD of 1 TM or less.

#### 3. The method of claim 2, wherein

20 R<sub>1</sub> is carboxylate, phosphonate, phosphate or sulfite and is connected to the ring with a 0 to 3 carbon linker,

 $R_2$  is H,

 $R_3$  is -I, -Br, or -CH<sub>3</sub>,

 $R_5$  is -I, -Br, or -CH<sub>3</sub>,

 $R_6$  is H,

R<sub>2</sub>' is H,

R<sub>3</sub>' is -I, -Br, -CH<sub>3</sub>, -iPr, -phenyl, benzyl, or 5- or 6-membered ring heterocycles,

 $R_4$ ' is -OH, -NH<sub>2</sub>, and -SH,

phosphonate, phosphate, sulfate, branched or straight chain alkyl having 1 to 9 carbons, substituted or unsubstituted aryl, wherein said substituted aryl is substituted with halogen or 1 to 5 carbon alkyl and wherein said aryl is optionally connected to the ring by a -CH<sub>2</sub>-, aromatic heterocycle having 5 to 6 atoms, wherein said heterocycle may be substituted with one or more groups selected from -OH, -NH<sub>2</sub>, -SH, -NH<sub>3</sub>, -N(CH<sub>3</sub>)<sub>3</sub>, carboxylate, phosphonate, phosphate or sulfate, heteroalkyl, arylalkyl, heteroaryl alkyl, polyaromatic, or polyheteroaromatic, wherein said R<sub>5</sub>' may be substituted with polar or charged groups, and

 $R_6$ ' is H.

- 4. The method of claim 1, wherein said compound fits spatially and preferentially into TR LBD isoform  $\alpha$  (TR- $\alpha$ ).
- 5. The method of claim 4, wherein said compound comprises an anionic group that interacts with the side chain oxygen or carbon of a serine residue corresponding to Ser277 of human TR-α, and wherein the anionic group is 1.7-4.0Å from the side chain atom.

6. The method of claim 1, wherein said compound fits spatially and preferentially into TR LBD isoform  $\beta$  (TR- $\beta$ ).

- The method of claim 6, wherein said compound comprises an anionic
   group that interacts with the side chain nitrogen of an arginine corresponding to
   Asn331 of human TR-β, and the anionic group is 1.7-4.0Å from the side chain atom.
- 8. A method for identifying a compound capable of selectively modulating the activity of a thyroid hormone receptor (TR) isoform, said method 10 comprising:

modeling test compounds that fit spacially and preferentially into a TR ligand binding domain (TR LBD) isoform of interest using an atomic structural model of a TR LBD isoform bound to a test compound,

screening said test compounds in a biological assay for TR isoform

15 activity characterized by binding of a test compound to a TR LBD isoform, and

identifying a test compound that selectively modulates the activity of a

TR isoform.

9. The method of claim 8, wherein said compound is of the formula:

25

which comprises the following substituents:

(i) an R<sub>1</sub>-substituent comprising an anionic group that interacts with a side chain nitrogen atom of an arginine corresponding to a residue selected from the group consisting of Arg228, Arg262, and Arg266 of human TR-α, and Arg282, Arg316 and
 5 Arg320 of human TR-β, and wherein the anionic group is 1.7-4.0Å from the nitrogen atom;

- (ii) an R<sub>2</sub>-substituent comprising a hydrophobic or hydrophilic group that fits spacially into the TR LBD;
- (iii) an R<sub>3</sub>-substituent comprising a hydrophobic or hydrophilic group that 10 interacts with a side chain atom of a serine, alanine or isoleucine corresponding to a residue selected from the group consisting of Ser260, Ala263 and Ile299 of human TR-α, and Ser314, Ala317 and Ile352 of human TR-β, and wherein the hydrophobic or hydrophilic group is 1.7-4.0Å from the side chain atom;
- (iv) an R<sub>5</sub>-substituent comprising a hydrophobic or hydrophilic group that 15 interacts with a side chain atom of a phenylalanine or isoleucine corresponding to a residue selected from the group consisiting of Phe218, Ile221 and Ile222 of human TR-α, and Phe272, Ile275 and Ile276 of human TR-β, and wherein the hydrophobic or hydrophilic group is 1.7-4.0Å from the side chain atom;
- (v) an R<sub>6</sub>-substituent comprising a hydrophobic or hydrophilic group that
   20 fits spacially into the TR LBD;
- (vi) an X-substituent comprising a hydrophobic or hydrophilic group that interacts with a side chain atom of a leucine corresponding to a residue selected from the group consisting of Leu276 and Leu292 of human TR-α, and Leu 330 and Leu346 of human TR-β, and wherein the hydrophobic or hydrophilic group is 1.7-4.0Å from 25 the side chain atom;

(vii) an R<sub>2</sub>'-substituent comprising a hydrophobic or hydrophilic group that fits spacially into the TR LBD;

- (viii) an R<sub>3</sub>'-substituent comprising a hydrophobic group that interacts with a side chain atom of a phenylalamine, glycine or methionine corresponding to a residue selected from the group consisting of Phe215, Gly290, and Met388 of human TR-α, and Phe269, Gly344, Met442 of human TR-β, and wherein the hydrophobic group is 1.7-4.0Å from the side chain atom;
- (ix) an R<sub>4</sub>'-substituent comprising an hydrogen bond donor or acceptor group that interacts with a side chain carbon or nitrogen atom of a histadine
   10 corresponding to residue His381 of human TR-α, and His435 of human TR-β, and wherein the hydrogen bond donor or acceptor group is 1.7-4.0Å from the side chain atom;
  - (x) an R<sub>5</sub>'-substituent comprising a hydrophobic or hydrophilic group that fits spacially into the TR LBD; and
- 15 (xi) and R<sub>6</sub>'-substituent comprising a hydrophobic or hydrophilic group that fits spacially into the TR LBD.
  - $10. \hspace{0.5cm} \text{The method according to claim 9,} \\$  wherein  $R_1$  is
- 20 -O-CH<sub>2</sub>CO<sub>2</sub>H, -NHCH<sub>2</sub>CO<sub>2</sub>H,
  - -CO<sub>2</sub>H, -CH<sub>2</sub>CO<sub>2</sub>H, -CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>H, -CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>H,
  - -CH<sub>2</sub>CH(NH<sub>2</sub>)CO<sub>2</sub>H,

-CH<sub>2</sub>CH[NHCOCH $\phi_2$ ]CO<sub>2</sub>H,

- -CH<sub>2</sub>CH[NHCO(CH<sub>2</sub>)<sub>15</sub>CH<sub>3</sub>
- $1CO_2H$ ,
- -CH<sub>2</sub>CH[NH-FMOC]CO<sub>2</sub>H,
- -CH<sub>2</sub>CH[NH-tBOC]CO<sub>2</sub>H, or a carboxylate connected to the ring with a 0 to 3
- 25 carbon linker,

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-PO<sub>3</sub>H<sub>2</sub>, -CH<sub>2</sub>PO<sub>3</sub>H<sub>2</sub>, -CH<sub>2</sub>CH<sub>2</sub>PO<sub>3</sub>H<sub>2</sub>, -CH<sub>2</sub>CHNH<sub>2</sub>PO<sub>3</sub>H<sub>2</sub>,
-CH<sub>2</sub>CH[NHCOCHφ<sub>2</sub>]PO<sub>3</sub>H<sub>2</sub>, -CH<sub>2</sub>CH[NHCO(CH<sub>2</sub>)<sub>15</sub>CH<sub>3</sub>]PO<sub>3</sub>H<sub>2</sub>,
-CH<sub>2</sub>CH[NH-FMOC]PO<sub>3</sub>H<sub>2</sub>, -CH<sub>2</sub> CH[NH-tBOC]PO<sub>3</sub>H<sub>2</sub>, or a phosphate or phosphonate connected to the ring with a 0 to 3 carbon linker,
```

-SO<sub>3</sub>H, -CH<sub>2</sub>SO<sub>3</sub>H, -CH<sub>2</sub>CH<sub>2</sub>SO<sub>3</sub>H, -CH<sub>2</sub>CHNH<sub>2</sub>SO<sub>3</sub>H,
-CH<sub>2</sub>CH[NHCOCHφ<sub>2</sub>]SO<sub>3</sub>H, -CH<sub>2</sub>CH[NHCO(CH<sub>2</sub>)<sub>15</sub>CH<sub>3</sub>]SO<sub>3</sub>H,
-CH<sub>2</sub>CH[NH-FMOC]SO<sub>3</sub>H, -CH<sub>2</sub> CH[NH-tBOC]SO<sub>3</sub>H, or a sulfate or sulfite

10 connected to the ring with a 0 to 3 carbon linker,

or acts as the functional equivalent of  $CH_2CH(NH_2)CO_2H$  of T3 in the molecular recognition domain when bound to a TR, wherein said  $R_1$  can be optionally substituted with an amine,

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wherein R2 is

H, halogen, CF<sub>3</sub>, OH, NH<sub>2</sub>, SH, CH<sub>3</sub>, -Et,

or acts as the functional equivalent of H in the molecular recognition domain when bound to a TR,

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wherein R<sub>3</sub> is

-H, halogen, -CF<sub>3</sub>, -OH, -NH<sub>2</sub>, -N<sub>3</sub>, -SH, -CH<sub>3</sub>, -Et, or acts as the functional equivalent of I in the molecular recognition domain when bound to a TR,

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wherein R<sub>5</sub> is

-H, halogen, -CF<sub>3</sub>, -OH, -NH<sub>2</sub>, -N<sub>3</sub>, -SH, -CH<sub>3</sub>, -Et, or acts as the functional equivalent of I in the molecular recognition domain when bound to a TR, and  $R_3$  can be identical to  $R_5$ ,

5

wherein R<sub>6</sub> is

-H, halogen, -CF<sub>3</sub>, -OH, -NH<sub>2</sub>, -SH, -CH<sub>3</sub>, or acts as the functional equivalent of H in the molecular recognition domain when bound to a TR, and  $R_2$  can be identical to  $R_6$ ,

10

wherein R2' is

-H, halogen, -CF<sub>3</sub>, -OH, -NH<sub>2</sub>, -N<sub>3</sub>, -SH, -CH<sub>3</sub>, -Et, or acts as the functional equivalent of H in the molecular recognition domain when bound to a TR,

15 wherein R<sub>3</sub>' is any hydrophobic group, including

halogen, -CF<sub>3</sub>, -SH, alkyl, aryl, 5- or 6-membered heterocyclie, cyano, or acts as the functional equivalent of I in the molecular recognition domain when bound to a TR,

#### 20 wherein R<sub>4</sub>' is

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-H, halogen, -CF<sub>3</sub>, -OH, -NH<sub>2</sub>, NH<sub>3</sub>, -N(CH<sub>3</sub>)<sub>3</sub>, carboxylate, phosphonate, phosphate or sulfate, -SH, -CH<sub>3</sub>, -Et, or akyl, aryl or 5- or 6-membered heterocyclic aromatic attached through urea or carbamate linkages to O or N or S at the R<sub>4</sub>' position, or acts as the functional equivalent of OH in the molecular recognition domain when bound to a TR,

wherein R<sub>5</sub>' is

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-H, -OH, -NH<sub>2</sub>, -N(CH<sub>3</sub>)<sub>2</sub> -SH -NH<sub>3</sub>, -N(CH<sub>3</sub>)<sub>3</sub>, carboxylate, phosphonate, phosphate, sulfate, branched or straight chain alkyl having 1 to 9 carbons, substituted or unsubstituted aryl, wherein said substituted aryl is substituted with halogen or 1 to 5 carbon alkyl and wherein said aryl is optionally connected to the ring by a -CH<sub>2</sub>-, aromatic heterocycle having 5 to 6 atoms, wherein said heterocycle may be substituted with one or more groups selected from -OH, -NH<sub>2</sub>, -SH, -NH<sub>3</sub>, -N(CH<sub>3</sub>)<sub>3</sub>, carboxylate, phosphonate, phosphate or sulfate, heteroalkyl, arylalkyl, heteroaryl alkyl, polyaromatic, or polyheteroaromatic, wherein said R<sub>5</sub>' may be substituted with polar or charged groups,

### wherein R<sub>6</sub>' is

-H, halogen, -CF<sub>3</sub>, -OH, -NH<sub>2</sub>, -SH, -CH<sub>3</sub>, -Et, or acts as the functional equivalent of H in the molecular recognition domain when bound to a TR,

### wherein X is

O, S, SO<sub>2</sub>, NH, NR<sub>7</sub>, CH<sub>2</sub>, CHR<sub>7</sub>, CR<sub>7</sub>R<sub>7</sub>, wherein R<sub>7</sub> is alkyl, aryl or 5- or 6-membered heterocyclic aromatic,

and wherein said TR LBD ligand has an apparent Kd for binding TR LBD of 1 TM or less.

25 11. The method of claim 10, wherein

R<sub>1</sub> is carboxylate, phosphonate, phosphate or sulfite and is connected to the ring with a 0 to 3 carbon linker,

R<sub>2</sub> is H,

 $R_3$  is -I, -Br, or -CH<sub>3</sub>,

 $R_5$  is -I, -Br, or -CH<sub>3</sub>,

R<sub>6</sub> is H,

R<sub>2</sub>' is H,

R<sub>3</sub>' is -I, -Br, -CH<sub>3</sub>, -iPr, -phenyl, benzyl, or 5- or 6-membered ring heterocycles,

 $R_4$ ' is -OH, -NH<sub>2</sub>, and -SH,

R<sub>5</sub>' is -H, -OH, -NH<sub>2</sub>, -N(CH<sub>3</sub>)<sub>2</sub> -SH -NH<sub>3</sub>, -N(CH<sub>3</sub>)<sub>3</sub>, carboxylate, phosphonate, phosphate, sulfate, branched or straight chain alkyl having 1 to 9 carbons, substituted or unsubstituted aryl, wherein said substituted aryl is substituted with halogen or 1 to 5 carbon alkyl and wherein said aryl is optionally connected to the ring by a -CH<sub>2</sub>-, aromatic heterocycle having 5 to 6 atoms, wherein said heterocycle may be substituted with one or more groups selected from -OH, -NH<sub>2</sub>, -SH, -NH<sub>3</sub>, -N(CH<sub>3</sub>)<sub>3</sub>, carboxylate, phosphonate, phosphate or sulfate, heteroalkyl, arylalkyl, heteroaryl alkyl, polyaromatic, or polyheteroaromatic, wherein said R<sub>5</sub>' may be substituted with polar or charged groups, and

 $R_6$ ' is H.

12. The method of claim 8, wherein said compound fits spatially and preferentially into TR LBD isoform  $\alpha$  (TR- $\alpha$ ).

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The method of claim 12, wherein said compound comprises an anionic group that interacts with the side chain oxygen or carbon of a serine residue corresponding to Ser277 of human TR- $\alpha$ , and wherein the anionic group is 1.7-4.0Å from the side chain atom.

5

- 14. The method of claim 8, wherein said compound fits spatially and preferentially into TR LBD isoform  $\beta$  (TR- $\beta$ ).
- 15. The method of claim 14, wherein said compound comprises an anionic 10 group that interacts with the side chain nitrogen of an arginine corresponding to Asn331 of human TR-β, and the anionic group is 1.7-4.0Å from the side chain atom.
  - 16. The method of claim 8, wherein said compound binds to a TR LBD isoform with greater affinity than thyronine or triidothyronine.

15

17. A method for identifying a thyroid hormone receptor (TR) agonist or antagonist ligand, said method comprising the steps of:

providing the atomic coordinates of a TR ligand binding domain (TR LBD) to a computerized modeling system;

20 modeling ligands which fit spacially into the TR LBD; and

identifying in a biological assay for TR activity a ligand which increases or descreases the activity of said TR, whereby a TR agonist or antagonist is identified.

18. A peptide, peptidomimetic or synthetic molecule identified by the method of any one of claims 8 or 17, with the proviso that said molecule is other than a thyronine or thyronine-like compound disclosed in a reference cited in Appendix I.

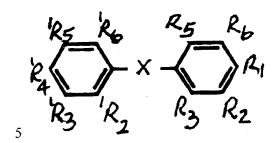
5 19. A method of identifying a compound that selectively modulates the activity of a thyroid hormone receptor (TR) compared to other nuclear hormone receptors, said method comprising:

modeling compounds which fit spacially into a TR ligand binding domain (TR LBD) using an atomic structural model of a TR LBD,

selecting a compound comprising conformationally constrained structural features that interact with conformationally constrained residues of a TR LBD,

identifying in a biological assay for TR activity a compound that selectively binds to a TR LBD compared to other nuclear receptors, whereby a compound that selectively modulates a TR is identified.

- 20. The method of claim 19, wherein said conformationally constrained residues of a TR LBD correspond to residues Met259, Leu276, Leu292, His381, Gly290, Ile221, and Phe401 of human TR-α, and residues Met313, Leu330, Leu346, 20 His435, Gly344, Ile275 and Phe455 of human TR-β.
  - 21. The method of claim 19, wherein said compounds are of the formula:



which comprises the following substituents:

- (i) an R<sub>1</sub>-substituent comprising an anionic group that interacts with a side chain nitrogen atom of an arginine corresponding to a residue selected from the group 10 consisting of Arg228, Arg262, and Arg266 of human TR-α, and Arg282, Arg316 and Arg320 of human TR-β, and wherein the anionic group is 1.7-4.0Å from the nitrogen atom;
  - (ii) an R<sub>2</sub>-substituent comprising a hydrophobic or hydrophilic group that fits spacially into the TR LBD;
- 15 (iii) an R<sub>3</sub>-substituent comprising a hydrophobic or hydrophilic group that interacts with a side chain atom of a serine, alanine or isoleucine corresponding to a residue selected from the group consisting of Ser260, Ala263 and Ile299 of human TR-α, and Ser314, Ala317 and Ile352 of human TR-β, and wherein the hydrophobic or hydrophilic group is 1.7-4.0Å from the side chain atom;
- 20 (iv) an R<sub>5</sub>-substituent comprising a hydrophobic or hydrophilic group that interacts with a side chain atom of a phenylalanine or isoleucine corresponding to a residue selected from the group consisting of Phe218, Ile221 and Ile222 of human TR-α, and Phe272, Ile275 and Ile276 of human TR-β, and wherein the hydrophobic or hydrophilic group is 1.7-4.0Å from the side chain atom;

(v) an R<sub>6</sub>-substituent comprising a hydrophobic or hydrophilic group that fits spacially into the TR LBD;

- (vi) an X-substituent comprising a hydrophobic or hydrophilic group that interacts with a side chain atom of a leucine corresponding to a residue selected from the group consisting of Leu276 and Leu292 of human TR-α, and Leu 330 and Leu346 of human TR-β, and wherein the hydrophobic or hydrophilic group is 1.7-4.0Å from the side chain atom;
  - (vii) an R<sub>2</sub>'-substituent comprising a hydrophobic or hydrophilic group that fits spacially into the TR LBD;
- 10 (viii) an R<sub>3</sub>'-substituent comprising a hydrophobic group that interacts with a side chain atom of a phenylalanine, glycine or methionine corresponding to a residue selected from the group consisting of Phe215, Gly290, and Met388 of human TR-α, and Phe269, Gly344, Met442 of human TR-β, and wherein the hydrophobic group is 1.7-4.0Å from the side chain atom;
- 15 (ix) an R<sub>4</sub>'-substituent comprising an hydrogen bond donor or acceptor group that interacts with a side chain carbon or nitrogen atom of a histidine corresponding to residue His381 of human TR-α, and His435 of human TR-β, and wherein the hydrogen bond donor or acceptor group is 1.7-4.0Å from the side chain atom;
- 20 (x) an R<sub>5</sub>'-substituent comprising a hydrophobic or hydrophilic group that fits spacially into the TR LBD; and
  - (xi) and R<sub>6</sub>'-substituent comprising a hydrophobic or hydrophilic group that fits spacially into the TR LBD.
- 25 22. The method of claim 19, wherein said compound comprises:

(i) a cyclic carbon atom that interacts with a carbon and oxygen atom of a methionine residue corresponding to Met259 of human TR- $\alpha$ , and Met313 of human TR- $\beta$ , wherein the cyclic carbon is about 3.0 to 4.0Å from the carbon and oxygen atom of the methionine;

- 5 (ii) a cyclic carbon atom that interacts with a carbon atom of a leucine residue corresponding to Leu276 of human TR-α, and Leu330 of human TR-β, wherein the cyclic carbon is about 3.0 to 4.0Å from the carbon atom of the leucine;
- (iii) a cyclic carbon atom that interacts with a carbon atom of a leucine residue corresponding to Leu292 of human TR-α, and Leu346 of human TR-β,
   10 wherein the cyclic carbon is about 3.0 to 4.0Å from the carbon atom of the leucine;
  - (iv) a  $R_3$ -substituent comprising an atom that interacts with a carbon atom of an isoleucine residue corresponding to Ile221 of human TR- $\alpha$ , and Ile275 of human TR- $\beta$ , wherein the R3-substituent atom is about 3.0 to 4.0Å from the carbon atom of the isoleucine;
- 15 (v) a  $R_3$ '-substituent comprising an atom that interacts with an oxygen atom of a glycine residue corresponding to Gly290 of human TR- $\alpha$ , and Gly344 of human TR- $\beta$ , wherein the R3'-substituent atom is about 3.0 to 4.0Å from the carbon atom of the glycine; and
- (vi) a R<sub>4</sub>'-substituent comprising an atom selected from the group 20 consisting of oxygen and carbon that interacts with (a) a carbon and nitrogen atom of a histidine residue corresponding to His381 of human TR-α, and His435 of human TR-β, wherein the R4'-substituent atom is about 2.0 to 4.0Å from the carbon atom of the histidine; and (b) a carbon atom of a phenylalanine residue corresponding to Phe401 of human TR-α, and human Phe455 of TR-β, wherein said atom is about 3.0 to 4.0Å from the carbon atom of the phenylalanine.

23. The method according to claim 21,

wherein R<sub>1</sub> is

-O-CH<sub>2</sub>CO<sub>2</sub>H, -NHCH<sub>2</sub>CO<sub>2</sub>H,

5 -CO<sub>2</sub>H, -CH<sub>2</sub>CO<sub>2</sub>H, -CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>H, -CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>H,

-CH<sub>2</sub>CH(NH<sub>2</sub>)CO<sub>2</sub>H,

-CH<sub>2</sub>CH[NHCOCH $\phi_2$ ]CO<sub>2</sub>H,

-CH<sub>2</sub>CH[NHCO(CH<sub>2</sub>)<sub>15</sub>CH<sub>3</sub>

 $CO_2H$ ,

-CH<sub>2</sub>CH[NH-FMOC]CO<sub>2</sub>H,

-CH<sub>2</sub>CH[NH-tBOC]CO<sub>2</sub>H, or a carboxylate connected to the ring with a 0 to 3

carbon linker,

10

 $-PO_3H_2$ ,  $-CH_2PO_3H_2$ ,

-CH<sub>2</sub>CH<sub>2</sub>PO<sub>3</sub>H<sub>2</sub>,

-CH<sub>2</sub>CHNH<sub>2</sub>PO<sub>3</sub>H<sub>2</sub>,

 $-CH_2CH[NHCOCH\phi_2]PO_3H_2$ ,

-CH<sub>2</sub>CH[NHCO(CH<sub>2</sub>)<sub>15</sub>CH<sub>3</sub>]PO<sub>3</sub>H<sub>2</sub>,

-CH<sub>2</sub>CH[NH-FMOC]PO<sub>3</sub>H<sub>2</sub>, -CH<sub>2</sub> CH[NH-tBOC]PO<sub>3</sub>H<sub>2</sub>, or a phosphate or

phosphonate connected to the ring with a 0 to 3 carbon linker,

15

 $-SO_3H$ ,  $-CH_2SO_3H$ ,

-CH<sub>2</sub>CH<sub>2</sub>SO<sub>3</sub>H,

-CH<sub>2</sub>CHNH<sub>2</sub>SO<sub>3</sub>H,

-CH<sub>2</sub>CH[NHCOCH $\phi_2$ ]SO<sub>3</sub>H,

-CH<sub>2</sub>CH[NHCO(CH<sub>2</sub>)<sub>15</sub>CH<sub>3</sub>]SO<sub>3</sub>H,

-CH2CH[NH-FMOC]SO3H, -CH2 CH[NH-tBOC]SO3H, or a sulfate or sulfate

connected to the ring with a 0 to 3 carbon linker,

20

or acts as the functional equivalent of CH<sub>2</sub>CH(NH<sub>2</sub>)CO<sub>2</sub>H of T3 in the molecular recognition domain when bound to a TR, wherein said R<sub>1</sub> can be optionally substituted with an amine,

25 wherein R<sub>2</sub> is

H, halogen, CF<sub>3</sub>, OH, NH<sub>2</sub>, SH, CH<sub>3</sub>, -Et,

or acts as the functional equivalent of H in the molecular recognition domain when bound to a TR,

# 5 wherein R<sub>3</sub> is

-H, halogen, -CF<sub>3</sub>, -OH, -NH<sub>2</sub>, -N<sub>3</sub>, -SH, -CH<sub>3</sub>, -Et,

or acts as the functional equivalent of I in the molecular recognition domain when bound to a TR,

### 10 wherein R<sub>5</sub> is

-H, halogen, -CF<sub>3</sub>, -OH, -NH<sub>2</sub>, -N<sub>3</sub>, -SH, -CH<sub>3</sub>, -Et, or acts as the functional equivalent of I in the molecular recognition domain when bound to a TR, and  $R_3$  can be identical to  $R_5$ ,

## 15 wherein R<sub>6</sub> is

-H, halogen, -CF<sub>3</sub>, -OH, -NH<sub>2</sub>, -SH, -CH<sub>3</sub>, or acts as the functional equivalent of H in the molecular recognition domain when bound to a TR, and  $R_2$  can be identical to  $R_6$ ,

### 20 wherein R<sub>2</sub>' is

-H, halogen, -CF<sub>3</sub>, -OH, -NH<sub>2</sub>, -N<sub>3</sub>, -SH, -CH<sub>3</sub>, -Et, or acts as the functional equivalent of H in the molecular recognition domain when bound to a TR,

wherein R<sub>3</sub>' is any hydrophobic group, including

halogen, -CF<sub>3</sub>, -SH, alkyl, aryl, 5- or 6-membered heterocycle, cyano, or acts as the functional equivalent of I in the molecular recognition domain when bound to a TR,

#### 5 wherein R<sub>4</sub>' is

-H, halogen, -CF<sub>3</sub>, -OH, -NH<sub>2</sub>, NH<sub>3</sub>, -N(CH<sub>3</sub>)<sub>3</sub>, carboxylate, phosphonate, phosphate or sulfate, -SH, -CH<sub>3</sub>, -Et, or akyl, aryl or 5- or 6-membered heterocyclic aromatic attached through urea or carbamate linkages to O or N or S at the R<sub>4</sub>' position, or acts as the functional equivalent of OH in the molecular recognition domain when bound to a TR,

#### wherein R<sub>5</sub>' is

10

15

20

-H, -OH, -NH<sub>2</sub>, -N(CH<sub>3</sub>)<sub>2</sub> -SH -NH<sub>3</sub>, -N(CH<sub>3</sub>)<sub>3</sub>, carboxylate, phosphonate, phosphate, sulfate, branched or straight chain alkyl having 1 to 9 carbons, substituted or unsubstituted aryl, wherein said substituted aryl is substituted with halogen or 1 to 5 carbon alkyl and wherein said aryl is optionally connected to the ring by a -CH<sub>2</sub>-, aromatic heterocycle having 5 to 6 atoms, wherein said heterocycle may be substituted with one or more groups selected from -OH, -NH<sub>2</sub>, -SH, -NH<sub>3</sub>, -N(CH<sub>3</sub>)<sub>3</sub>, carboxylate, phosphonate, phosphate or sulfate, heteroalkyl, arylalkyl, heteroaryl alkyl, polyaromatic, or polyheteroaromatic, wherein said R<sub>5</sub>' may be substituted with polar or charged groups,

wherein R<sub>6</sub>' is

-H, halogen, -CF<sub>3</sub>, -OH, -NH<sub>2</sub>, -SH, -CH<sub>3</sub>, -Et, or acts as the functional equivalent of H in the molecular recognition domain when bound to a TR,

wherein X is

5 O, S, SO<sub>2</sub>, NH, NR<sub>7</sub>, CH<sub>2</sub>, CHR<sub>7</sub>, CR<sub>7</sub>R<sub>7</sub>, wherein R<sub>7</sub> is alkyl, aryl or 5- or 6-membered heterocyclic aromatic,

and wherein said TR LBD ligand has an apparent Kd for binding TR LBD of 1 TM or less.

10

25

24. The method of claim 23, wherein

 $R_1$  is carboxylate, phosphonate, phosphate or sulfite and is connected to the ring with a 0 to 3 carbon linker,

R<sub>2</sub> is H,

15  $R_3$  is -I, -Br, or -CH<sub>3</sub>,

 $R_5$  is -I, -Br, or -CH<sub>3</sub>,

R<sub>6</sub> is H,

R<sub>2</sub>' is H,

 $R_3$ ' is -I, -Br, -CH $_3$ , -iPr, -phenyl, benzyl, or 5- or 6-membered ring 20 heterocycles,

R<sub>4</sub>' is -OH, -NH<sub>2</sub>, and -SH,

R<sub>5</sub>' is -H, -OH, -NH<sub>2</sub>, -N(CH<sub>3</sub>)<sub>2</sub> -SH -NH<sub>3</sub>, -N(CH<sub>3</sub>)<sub>3</sub>, carboxylate, phosphonate, phosphate, sulfate, branched or straight chain alkyl having 1 to 9 carbons, substituted or unsubstituted aryl, wherein said substituted aryl is substituted with halogen or 1 to 5 carbon alkyl and wherein said aryl is

optionally connected to the ring by a -CH<sub>2</sub>-, aromatic heterocycle having 5 to 6 atoms, wherein said heterocycle may be substituted with one or more groups selected from -OH, -NH<sub>2</sub>, -SH, -NH<sub>3</sub>, -N(CH<sub>3</sub>)<sub>3</sub>, carboxylate, phosphonate, phosphate or sulfate, heteroalkyl, arylalkyl, heteroaryl alkyl, polyaromatic, or polyheteroaromatic, wherein said  $R_5$ ' may be substituted with polar or charged groups, and

R<sub>6</sub>' is H.

- 25. The method of claim 19, wherein said compound fits spatially and 10 preferentially into TR LBD isoform  $\alpha$  (TR- $\alpha$ ).
- 26. The method of claim 25, wherein said compound comprises an anionic group that interacts with the side chain oxygen or carbon of a serine residue corresponding to Ser277 of human TR-α, and wherein the anionic group is 1.7-4.0Å from the side chain atom.
  - 27. The method of claim 19, wherein said compound fits spatially and preferentially into TR LBD isoform  $\beta$  (TR- $\beta$ ).
- 28. The method of claim 27, wherein said compound comprises an anionic group that interacts with the side chain nitrogen of an arginine corresponding to Asn331 of human TR-β, and the anionic group is 1.7-4.0Å from the side chain atom.
- 29. The method of claim 19, wherein said compound binds to a TR LBD 25 isoform with greater affinity than thyronine or triiodothyronine.

30. The method of claim 1, wherein said compound comprises a cyclic carbon atom that interacts with a carbon and oxygen atom of a methionine residue corresponding to Met259 of human TR-I, and Met313 of human TR-β, wherein the 5 cyclic carbon is about 3.0 to 4.0Å from the carbon and oxygen atom of the methionine.

31. The method of claim 30, wherein said cyclic carbon is inner ring carbon C11.

10

32. The method of claim 1, wherein said compound comprises a cyclic carbon atom that interacts with a carbon atom of a leucine residue corresponding to Leu276 of human TR- $\alpha$ , and Leu330 of human TR- $\beta$ , wherein the cyclic carbon is about 3.0 to 4.0Å from the carbon atom of the leucine.

- 33. The method of claim 32, wherein said cyclic carbon is selected from the group consisting of inner ring carbons C7 and C9.
- 34. The method of claim 1, wherein said compound comprises a cyclic 20 carbon atom that interacts with a carbon atom of a leucine residue corresponding to Leu292 of human TR-α, and Leu346 of human TR-β, wherein the cyclic carbon is about 3.0 to 4.0Å from the carbon atom of the leucine.
- 35. The method of claim 34, wherein said cyclic carbon is selected from 25 the group consisting of outer ring carbons C6 and C8.

36. The method of claim 1, wherein said R<sub>3</sub>-substituent comprises an atom that interacts with a carbon atom of an isoleucine residue corresponding to Ile221 of human TR-α, and Ile275 of human TR-β, wherein the R<sub>3</sub>-substituent atom is about 5 3.0 to 4.0Å from the carbon atom of the isoleucine.

- 37. The method of claim 1, wherein said R<sub>3</sub>'-substituent comprises an atom that interacts with an oxygen atom of a glycine residue corresponding to Gly290 of human TR-α, and Gly344 of human TR-β, wherein the R<sub>3</sub>'-substituent atom is 10 about 3.0 to 4.0Å from the carbon atom of the glycine.
- 38. The method of claim 1, wherein said R<sub>4</sub>'-substituent comprises an atom selected from the group consisting of oxygen and carbon that interacts with a carbon and nitrogen atom of a histidine residue corresponding to His381 of human 15 TR-α, and His435 of human TR-β, wherein the R<sub>4</sub>'-substituent atom is about 2.0 to 4.0Å from the carbon atom of the histidine.
- 39. The method of claim 1, wherein said R<sub>4</sub>'-substituent comprises an oxygen atom that interacts with a carbon atom of a phenylalanine residue 20 corresponding to Phe401 of human TR-α, and human Phe455 of TR-β, wherein said atom is about 3.0 to 4.0Å from the carbon atom of the phenylalanine.
- 40. A method for identifying a thyroid hormone receptor (TR) agonist or antagonist ligand that selectively modulates the activity of a TR compared to other nuclear receptors, said method comprising the steps of:

providing the atomic coordinates of a TR ligand binding domain (TR LBD) to a computerized modeling system;

modeling ligands which fit spacially into the TR LBD and which interact with conformationally constrained residues of a TR LBD conserved among 5 TR isoforms; and

identifying in a biological assay for TR activity a ligand which selectively binds to said TR and increases or decreases the activity of said TR, whereby a TR agonist or antagonist that selectively modulates the activity of a TR is identified.

- 41. A peptide, peptidomatic or synthetic molecule identified by the method of any one of claims 19 or 40, with the proviso that said molecule is other than a thyronine or thyronine-like compound disclosed in a reference cited in Appendix I.
- 15 42. A machine-readable data storage medium, comprising a data storage material encoded with machine readable data which, when using a machine programmed with instructions for using said data, is capable of displaying a graphical three-dimensional representation of a molecule or molecular complex for a thyroid hormone ligand binding pocket comprising structure coordinates of TR-α amino acids 20 corresponding to human TR-α amino acids Met259, Leu276, and Ile221, or a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

43. A machine-readable data storage medium, comprising a data storage material encoded with machine readable data which, when using a machine programmed with instructions for using said data, is capable of displaying a graphical three-dimensional representation of a molecule or molecular complex for a thyroid 5 hormone ligand binding pocket comprising structure coordinates of TR-α amino acids corresponding to human TR-α amino acids Leu292, His381, Gly290 and Phe401, or a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

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44. The machine-readable storage medium according to any one of claims 42 or 43, wherein said binding pocket comprises structure coordinates of TR- $\alpha$  amino acids corresponding to human TR- $\alpha$  amino acids Met259, Leu276, Leu292, His381, Gly290, Ile221 and Phe401.

- 45. The machine-readable storage medium according to claim 44, wherein said binding pocket comprises structure coordinates of TR- $\alpha$  amino acids corresponding to human TR- $\alpha$  amino acids Arg228, Arg262 and Arg266.
- 20 46. The machine-readable storage medium according to claim 44, wherein said binding pocket comprises structure coordinates of TR-α amino acids corresponding to human TR-α amino acids Ser260, Ala263 and Ile299.

47. The machine-readable storage medium according to claim 44, wherein said binding pocket comprises structure coordinates of  $TR-\alpha$  amino acids corresponding to human  $TR-\alpha$  amino acids Phe218, Ile221 and Ile222.

- 5 48. The machine-readable storage medium according to claim 44, wherein said binding pocket comprises structure coordinates of TR-α amino acids corresponding to human TR-α amino acids Phe215, Gly290 and Met388.
- 49. The machine-readable storage medium according to claim 44, wherein 10 said binding pocket comprises structure coordinates of a TR-α amino acid corresponding to human TR-α amino acid Ser277.
- 50. A machine-readable data storage medium, comprising a data storage material encoded with machine readable data which, when using a machine programmed with instructions for using said data, is capable of displaying a graphical three-dimensional representation of a molecule or molecular complex for a thyroid hormone ligand binding pocket comprising structure coordinates of TR-β amino acids corresponding to human TR-β amino acids Met313, Leu330, and Ile275, or a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.
- 51. A machine-readable data storage medium, comprising a data storage material encoded with machine readable data which, when using a machine 25 programmed with instructions for using said data, is capable of displaying a graphical

three-dimensional representation of a molecule or molecular complex for a thyroid hormone ligand binding pocket comprising structure coordinates of TR-β amino acids corresponding to human TR-β amino acids Leu346, His435, Gly344, and Phe455, or a homologue of said molecule or molecular complex, wherein said homologue comprises a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

- 52. The machine-readable data storage medium according to any one of claims 50 or 51, wherein said binding pocket comprises structure coordinates of TR-β
   10 amino acids corresponding to human TR-β amino acids Met313, Leu330, Leu346, His435, Gly344, Ile275 and Phe455.
- 53. The machine-readable data storage medium according to claim 52, wherein said binding pocket comprises structure coordinates of TR-β amino acids 15 corresponding to human TR-β amino acids Arg282, Arg316 and Arg320.
  - 54. The machine-readable data storage medium according to claim 52, wherein said binding pocket comprises structure coordinates of TR-β amino acids corresponding to human TR-β amino acids Ser314, Ala317 and Ile352.

20

55. The machine-readable data storage medium according to claim 52, wherein said binding pocket comprises structure coordinates of TR- $\beta$  amino acids corresponding to human TR- $\beta$  amino acids Phe272, Ile275 and Ile276.

56. The machine-readable data storage medium according to claim 52, wherein said binding pocket further comprises structure coordinates of TR-β amino acids corresponding to human TR-β amino acids Phe269, Gly344 and Met442.

- 5 57. The machine-readable data storage medium according to claim 52, wherein said binding pocket comprises structure coordinates of a TR-β amino acid corresponding to human TR-β amino acid Asn331.
- 58. The machine-readable data storage medium according to claim 52, 10 wherein said molecule or molecular complex is defined by the set of structure coordinates selected from the group consisting coordinates depicted in Appendix 3, 4, 5 and 6, or a homologue of said molecule or molecular complex, said homologue having a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

- 59. The machine-readable data storage medium according to claim 52, wherein said molecule or molecular complex is defined by the set of structure coordinates selected from the group consisting coordinates depicted in Appendix 7 and 8, or a homologue of said molecule or molecular complex, said homologue 20 having a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.
- 60. A machine-readable data storage medium comprising a data storage material encoded with a first set of machine readable data which, when combined 25 with a second set of machine readable data, using a machine programmed with

instructions for using said first set of data and said second set of data, can determine at least a portion of the structure coordinates corresponding to the second set of machine readable data, wherein: said first set of data comprises a Fourier transform of at least a portion of the structural coordinates selected from the group consisting of coordinates depicted in Appendix 3, 4, 5, 6, 7 and 8; and said second set of data comprises an X-ray diffraction pattern of a molecule or molecular complex.

### APPENDIX 1

Andrea, T.A., et al. J Med Chem 22, 221-232 (1979).

Andrews et al, U.S. Patent No. 4,741,897, issued May 3, 1989.

Apriletti, J.W., Baxter, J.D., Lau, K.H & West, B.L. Protein Expression and

5 Purification 6, 363-370 (1995).

Apriletti, J.W., Baxter, J.D. & Lavin, T.N. J. Biol. Chem. 263, 9409-9417 (1988).

Au-Fliegner, M., Helmer, E., Casanova, J., Raaka, B.M. & Samuels, H.H. *Mol Cell Biol* 13, 5725-5737 (1993).

10 Baniahmad, A., et al. Mol Cell Biol 15, 76-86 (1995).

Barettino, D., Vivanco Ruiz, M.M. & Stunnenberg, H.G. *Embo J* 13, 3039-3049 (1994).

Beck-Peccoz, P., et al. J Clin Endocrinol Metab 78, 990-993 (1994).

Bhat, M.K., McPhie, P. & Cheng, S.Y. Biochem Biophys Res Commun 210,

15 464-471 (1995).

Blake, C.C. & Oatley, S.J. Nature 268, 115-120 (1977).

Blake, C.C., Geisow, M.J., Oatley, S.J., Rerat, B. & Rerat, C. *J Mol Biol* 121, 339-356 (1978).

Bourguet, W., Ruff, M., Chambon, P., Gronemeyer, H. & Moras, D. Nature

20 **375**, 377-382 (1995).

Brent, G.A. N Engl J Med 331, 847-853 (1994).

Brunger, A.T., Kuriyan, J. & Karplus, M. Science 235, 458-460 (1987).

Casanova, J., et al. Mol Cell Biol 14, 5756-5765 (1994).

Cavailles, V., et al. Embo J 14, 3741-3751 (1995).

25 Chin et al, U.S. Patent No. 5,284,999, issued February 8, 1994.

Collaborative Computational Project, N.4. Acta Crystallogr. **D50**, 760-763 (1994).

Collingwood, T.N., Adams, M., Tone, Y & Chatterjee, V.K. Mol Endocrinol 8, 1262-1277 (1994).

5 Cowtan, K. Joint CCP4 and ESF-EACBM Newsletter on Protein Crystallography 31, 34-38 (1994).

Damm, K. & Evans, R.M. Proc Natl Acad Sci USA 90, 10668-10672 (1993).

Danielian, P.S., White, R., Lees, J.A. & Parker, M.G. *Embo J* 11, 1025-1033 (1992).

Davies et al, U.S. Patent No. 5,322,933, issued June 21, 1994.

Dawson et al, U.S. Patent No. 5,466,861, issued November 14, 1995.

DeGroot et al, U.S. Patent No. 5,438,126, issued August 1, 1995.

Dietrich, S.W., Bolger, M.B., Kollman, P.A. & Jorgensen, E.C. J Med Chem **20**, 863-880 (1977).

Durand, B., et al. Embo J 13, 5370-5382 (1994).

Ellis et al, U.S. Patent No. 4,766,121, issued August 23, 1988.

Ellis et al, U.S. Patent No. 4,826,876, issued May 2, 1989.

Ellis et al, U.S. Patent No. 4,910,305, issued March 20, 1990.

Emmett et al, U.S. Patent No. 5,061,798, issued October 29, 1991.

20 Evans, R.M. Science 240, 889-895 (1988).

Evans et al. U.S. Patent No. 5,171,671, issued December 15, 1992.

Evans et al, U.S. Patent No. 5,312,732, issued May 17, 1994.

Fawell, S.E., Lees, J.A., White, R. & Parker, M.G. Cell 60, 953-962 (1990).

Forman, B.M. & Samuels, H.H. Mol. Endocrinol. 4, 1293-1301 (1990).

Gewirth, D.T. & Sigler, P.B. Nature Structural Biology 2, 386-394 (1995).

Glass, C.K. Endocr Rev 15, 391-407 (1994).

Hayashi, Y. Sunthornthepvarakul, T. & Refetoff, S. *J Clin Invest* **94**, 607-615 (1994).

Jones, T.A., Zou, J.Y., Cowan, S.W. & Kjeldgaard. Acta Crystallogr A 47,

5 110-119 (1991).

Jorgensen, E.C. in *Hormonal Peptides and Proteins* (eds. Li, C.H.) 107-204 (Academic Press, New York, 1978).

Kabsch, W. J. Appl. Crystallogr. 26, 795-800 (1993).

Kabsch, W. & Sander, C. Biopolymers 22, 2577-2637 (1983).

10 Laskowski, R.A., Macarthur, M.W., Moss, D.S. & Thornton, J.M. J. Appl. Crystallogr. 26, 283-291 (1993).

Latham, K.R., Apriletti, J.W., Eberhardt, N.L. & Baxter, J.D. *J Biol Chem* **256**, 12088-12093 (1981).

Laudet, V., Hanni, C., Coll, J., Catzeflis, F. & Stehelin, D. Embo J 11, 1003-

15 1013 (1992).

LeDouarin, B., et al. Embo J 14, 2020-2033 (1995).

Lee, J.W., Ryan, F., Swaffield, J.C., Johnston, S.A. & Moore, D.D. *Nature* 374, 91-94 (1995).

Lee, J.W., Choi, H.S., Gyuris, J., Brent, R. & Moore, D.D. Molec. Endocrinol.

**9**, 243-254 (1995).

25

Leeson, P.D., Emmett, J.C., Shah, V.P., Showell, G.A., Novelli, R., Prain, H.D., Benson, M.G., Ellis, D., Pearce, N.J. & Underwood, A.H. J. Med. Chem. 32, 320-336 (1989).

Leeson, P.D., Ellis, D., Emmett, J.D., Shah, V.P., Showell, G.A. & Underwood, A.H. J. Leng, X., et al. Mol Cell Biol 15, 255-263 (1995).

Leng, X., Tsai, S.Y., O'Malley, B.W. & Tsai, M.J. J Steroid Biochem Mol Biol 46, 643-661 (1993).

Lin, K.H., Parkison, C., McPhie, P. & Cheng, S.Y. Mol. Endocrinol. 5, 485-492 (1991).

5 Luisi, B.F., et al. Nature **352**, 497-505 (1991).

McGrath, M.E., et al. J. Mol. Biol. 237, 236-239 (1994).

McRee, D.E., *Practical Protein Crystallography*, Academic Press, N.Y. (1993), especially chapters 1, 2 and 3.

Meier, C.A., et al. Mol. Endocrinol. 6, 248-258 (1992).

- 10 Miura et al, U.S. Patent No. 5,116,828, issued May 26, 1992.
  - Monaco, H.L., Rizzi, M. & Coda, A. Science 268, 1039-1041 (1995).

Nicholls, A., Sharp, K.A. & Honig, B. Proteins 11, 281-296 (1991).

- O'Donnell, A.L., Rosen, E.D., Darling, D.S. & Koenig, R.J. *Mol. Endocrinol.* 5, 94-99 (1991).
- Otwinowski, Z. Proceedings of the CCP4 Study Weekend 80-86 (SERC Daresbury Laboratory, Warrington, U.K., 1991).
  - Otwinowski, Z. Proceedings of the CCP4 Study Weekend: "Data Collection and Processing" 56-62 (SERC Daresbury Laboratory, Warrington, U.K., 1993).
- Ozato, U.S. Patent No. 5,403,925, issued April 4, 1995.

Rastinejad, R., Perlmann, T., Evans, R.M. & Sigler, P.B. *Nature* **375**, 203-211 (1995).

Refetoff, S., Weiss, R.E. & Usala, S.J. Endocr. Rev. 14, 348-399 (1993).

Ribeiro, R.C.J., Kushner, P.J. & Baxter, J.D. Annu. Rev. Med. 46, 443-453

25 (1995).

Ribeiro, R.C.J., et al. Ann. N. Y. Acad. Sci. 758, 366-389 (1995).

Ribeiro, R.C., Kushner, P.J., Apriletti, J.W., West, B.L. & Baxter, J.D. *Mol. Endocrinol.* **6**, 1142-1152 (1992).

Saatcioglu, F., Bartunek, P., Deng, T., Zenke, M. & Karin, M. Mol. Cell Biol. 13, 3675-3685 (1993).

Schwabe, J.W., Chapman, L., Finch, J.T. & Rhodes, D. Cell 75, 567-578 (1993).

Selmi, S. & Samuels, H.H. J. Biol. Chem. 266, 11589-11593 (1991).

Swaffield, J.C., Melcher, K. & Johnston, S.A. Nature 374, 88-91 (1995).

10 Toney, J.H. et al. Biochemistry 32, 2-6 (1993).

5

Tsai, M.J. & O'Malley, B.W. Annu. Rev. Biochem. 63, 451-486 (1994).

Zenke, M., Munoz, A., Sap, J., Vennstrom, B. & Beug, H. Cell 61, 1035-1049 (1990).

## **APPENDIX 2**

Table 8

Dimit	Amino Acid	Amino Acid	<u>Distance</u>
Atom	in full length $\alpha$	Atom	Å
C16	215-PHE	CD1	3.98
C16	215-PHE	CE1	3.86
C19	218-PHE	О	3.69
C16	218-PHE	СВ	3.89
C18	218-PHE	CB	3.92
C19	218-PHE	СВ	4.13
C18	218-PHE	CD2	3.77
C16	219-THR	CG2	3.68
C19	221-ILE	CG1	4.11
C6	222-ILE	CD1	4.18
C8	222-ILE	CD1	3.72
C10	222-ILE	CD1	3.53
C12	222-ILE	CD1	3.85
O1	222-ILE	CD1	4.13
C13	225-ALA	C8	3.64
O4	225-ALA	C8	4.02
04	228-ARG	CZ	3.96
C17	228-ARG	NH2	3.36
O3	228-ARG	NH2	3.58
04	228-ARG	NH2	2.86
C10	256-MET	SD	3.70
C12	256-MET	SD	3.89
C10	256-MET	CE	3.88
C12	256-MET	CE	3.83
C11	259-MET	С	4.03
C11	259-MET	O	3.66
C15	259-MET	0	3.42
N1	259-MET	O	3.71
C1	259-MET	C8	4.20
C11	259-MET	C8	3.87
C13	259-MET	C8	4.09
C15	262-ARG	C8	4.03
C17	262-ARG	C8	3.58
O3	262-ARG	C8	3.62
04	262-ARG	C8	3.85
C17	262-ARG	CD	4.10
O4	262-ARG	CD	3.61
N1	263-ALA	N	3.71
C17	263-ALA	CA	3.69
N1	263-ALA	СВ	3.46
O3	266-ARG	NH1	3.93

Dimit	Amino Acid	Amino Acid	Distance
Atom	in full length α	Atom	Å
N1	275-THR	O	3.62
N1	276-LEU	CA	3.51
N1	276-LEU	C	3.92
C5	276-LEU	CD1	4.05
C19	276-LEU	CD1	4.04
C7	276-LEU	CD2	4.09
C9	276-LEU	CD2	3.95
C11	276-LEU	CD2	4.13
N1	276-LEU	CD2	4.17
C13	277-SER	N	4.14
C15	277-SER	N	3.79
C17	277-SER	N	3.69
N1	277-SER	N	3.30
O3	277-SER	N	3.19
C17	277-SER	CA	3.92
O3	277-SER	CA	3.35
C13	277-SER	OG	3.92
C7	287-LEU	CD2	3.90
C18	290-GLY	C	4.04
C18	290-GLY	0	3.54
C18	291-GLY	CA	4.04
C18	292-LEU	N	4.20
C2	292-LEU	CG	4.18
C4	292-LEU	CG	3.86
C6	292-LEU	CG	4.01
C2	292-LEU	CD1	3.88
C4	292-LEU	CD1	4.02
O2	292-LEU	CD1	4.07
C4	292-LEU	CD2	4.05
C6	292-LEU	CD2	3.72
C8	292-LEU	CD2	3.69
C10	292-LEU	CD2	3.98
O1	292-LEU	CD2	4.16
C20	299-ILE	CD1	3.87
C8	381-HIS	CD2	3.90
C10	381-HIS	CD2	3.84
O1	381-HIS	GO2	3.40
O1	381-HIS	CE1	3.72
C8	381-HIS	NE2	3.47
C10	381-HIS	NE2	3.51
O1	381-HIS	NE2	2.64
C6	388-MET	CE	3.90
C8	401-PHE	CE1	4.19
O1	401-PHE	CE1	3.37

Dimit	Amino Acid	Amino Acid	Distance
Atom	in full length α	Atom	Å
C16	401-PHE	CZ	3.97
O1	401-PHE	CZ	3.28
N1	502-H <sub>2</sub> O	O1	3.35
O3	502-H <sub>2</sub> O	O1	2.56
O3	503-H <sub>2</sub> O	01	3.13
O4	503-H <sub>2</sub> O	01	3.72
O4	504-H <sub>2</sub> O	01	2.72

Legend to Table 8. The table lists the interactions with Dimit (DMT). The column headings are as follows:

- #1 The atom of Dimit that interacts with the amino acid of the receptor. These are also 5 numbered in Figure 32.
- #2 The amino acid in the full length rTR\alpha that interacts with the ligand.
- #3 The name of the atom in the amino acid (standard nomenclature) where the interaction occurs.
- #4 The distance in Å between Dimit and the protein atom.

Table 9

Triac	Amino Acid	Amino Acid	
Atom	in full length α	Atom	Distance Å
I1	218-PHE	0	3.52
<u> </u>	221-ILE	CD1	4.16
<u> </u>	221-ILE	CG1	3.92
I1	222-ILE	CA	4.15
<u> </u>	222-ILE	СВ	4.03
<u> </u>	222-ILE	CG1	3.92
C8	222-ILE	CD1	4.12
C10	222-ILE	CD1	3.77
C12	222-ILE	CD1	3.79
C13	225-ALA	CB	4.17
C3	225-ALA	СВ	3.86
C10	256-MET	SD	3.45
C12	256-MET	SD	3.73
C10	256-MET	CE	3.66
C12	256-MET	CE	3.77
I3	256-MET	CE	3.89
C1	259-MET	O	3.93
C11	259-MET	0	3.24
O3	259-MET	О	4.09
C1	259-MET	СВ	3.89
C13	259-MET	0	3.74
C14	259-MET	О	3.96
C1	259-MET	CB	3.89
C11	259-MET	CB	3.68
C13	259-MET	CB	4.01
C11	259-MET	CA	4.13
C13	259-MET	CA	4.20
I3	260-SER	CA	4.10
I3	260-SER	OG	4.19
C14	262-ARG	CB	4.07
O4	262-ARG	СВ	3.60
O3	263-ALA	N	3.79
C14	263-ALA	N	4.12
O3	263-ALA	CA	3.67
O3	263-ALA	СВ	3.49
C11	263-ALA	СВ	4.00
C14	266-ARG	CZ	3.89
03	266-ARG	CZ	4.01
04	266-ARG	CZ	3.03
C14	266-ARG	NH1	3.25
O3	266-ARG	NH1	3.00
04	266-ARG	NH1	2.82

Triac	Amino Acid	Amino Acid	
Atom	in full length α	Atom	Distance Å
C14	266-ARG	NH2	3.48
03	266-ARG	NH2	4.01
04	266-ARG	NH2	2.34
03	275-THR	С	4.02
C14	275-THR	O	4.20
O3	275-THR	O	3.20
O3	278-LEU	CA	3.11
03	276-LEU	С	3.52
O3	276-LEU	N	4.04
C14	276-LEU	CA	3.98
O3	276-LEU	CA	3.11
C14	276-LEU	C	3.98
O3	276-LEU	CB	3.95
O2	276-LEU	CD1	4.03
I1	276-LEU	CD1	4.10
C7	276-LEU	CD2	3.84
C9	276-LEU	CD2	3.73
CII	276-LEU	CD2	4.06
O2	276-LEU	CD2	4.10
03	276-LEU	CD2	3.91
C13	277-SER	N	4.06
C14	277-SER	N	3.13
O4	277-SER	N	3.28
O3	277-SER	N	3.05
C14	277-SER	CA	3.76
O4	277-SER	CA	3.52
C3	277-SER	OG	3.87
C13	277-SER	OG	4.02
C14	277-SER	OG	4.14
I2	290-GLY	О	3.57
12	292-LEU	CG	3.94
C4	292-LEU	CG	3.95
C6	292-LEU	CG	3.65
C8	292-LEU	CG	4.02
C2	292-LEU	CD1	4.11
C4	292-LEU	CD1	3.85
C6	292-LEU	CD1	4.02
I2	292-LEU	CD2	3.98
C4	292-LEU	CD2	4.11
C6	292-LEU	CD2	3.44
C8	292-LEU	CD2	3.28
C10	292-LEU	CD2	3.88
O1	292-LEU	CD2	3.35
I3	299-ILE	CD1	3.77

Triac	Amino Acid	Amino Acid	
Atom	in full length α	Atom	Distance Å
C8	381-HIS	CD2	3.87
C10	381-HIS	CD2	3.90
O1	381-HIS	GO2	3.20
O1	381-HIS	CE1	3.82
C8	381-HIS	NE2	3.57
C10	381-HIS	NE2	3.52
O1	381-HIS	NE2	2.64
01	388-MET	CE	4.03
O1	401-PHE	CE1	3.86
01	401-PHE	CZ	3.70
C13	460-H <sub>2</sub> 0	01	4.00

Legend to Table 9. The table lists the interactions with Triac. The column headings are as follows:

<sup>#1</sup> The atom of Triac that interacts with the amino acid of the receptor. These are also 5 numbered in Figure 32.

<sup>#2</sup> The amino acid in the full length rTR $\alpha$  that interacts with the ligand.

<sup>#3</sup> The name of the atom in the amino acid (standard nomenclature) where the interaction occurs.

<sup>#4</sup> The distance in Å between Triac and the protein atom.

Table 10

IpBR <sub>2</sub> Atom	Amino Acid	Amino Acid	Distance
_1	in full length α	Atom	Å
C16	215-PHE	CD1	4.01
C16	215-PHE	CE1	3.78
BR1	218-PHE	0	3.24
BR1	218-PHE	C	3.98
C16	218-PHE	СВ	3.81
C18	218-PHE	СВ	3.92
BR1	218-PHE	CB	4.08
C18	218-PHE	CD2	3.92
C16	219-THR	CG2	3.45
BR1	221-ILE	CG1	3.81
BR1	221-ILE	CD1	4.07
BR1	222-ILE	CB	3.81
BR1	222-ILE	CG1	3.97
C6	222-ILE	CD1	4.07
C8	222-ILE	CD1	3.64
C10	222-ILE 222-ILE	CD1	3.50
C10	222-ILE 222-ILE	CD1	3.82
01	222-ILE 222-ILE	CD1	4.08
C13	225-ALA	CB	3.76
04	225-ALA 225-ALA	CB	4.01
04	228-ARG	CZ	3.92
C17	228-ARG	NH2	3.26
03	228-ARG	NH2	3.43
	228-ARG	NH2	2.79
04	256-MET	SD	3.65
C10	1	SD	3.71
C12	256-MET	CE	3.90
C10	256-MET	CE	3.75
C12	256-MET	CE	4.03
BR2	256-MET	CE	3.98
C11	259-MET	0	3.52
C11	259-MET	0	3.44
C15	259-MET		3.76
N1	259-MET	0	
C11	259-MET	СВ	3.87
N1	262-ARG	C	4.03
C15	262-ARG	CB	4.03
C17	262-ARG	CB	3.56
03	262-ARG	СВ	3.55
04	262-ARG	CB	3.91
C17	262-ARG	CD	4.09
04	262-ARG	CD	3.71
N1	263-ALA	N	3.61

IpBR <sub>2</sub> Atom	Amino Acid	Amino Acid	Distance
-r	in full length α	Atom	Å
N1	263-ALA	CA	3.59
N1	263-ALA	СВ	3.54
03	266-ARG	NH1	3.93
N1	275-THR	0	3.43
N1	276-LEU	CA	3.46
N1	276-LEU	C	3.83
C5	276-LEU	CD1	4.02
C7	276-LEU	CD2	4.00
C9	276-LEU	CD2	3.81
C11	276-LEU	CD2	3.91
C13	277-SER	N	3.79
C15	277-SER	N	3.63
C17	277-SER	N	3.70
N1	277-SER	N	3.17
03	277-SER	N	3.37
C17	277-SER	CA	3.89
03	277-SER	CA	3.43
C13	277-SER	OG	3.66
02	287-LEU	CD1	4.05
C18	290-GLY	C	4.04
C18	290-GLY	O	3.48
C18	291-GLY	CA	4.02
C4	292-LEU	CG	3.89
C6	292-LEU	CG	4.02
C2	292-LEU	CD1	3.79
C4	292-LEU	CD1	3.96
02	292-LEU	CD1	3.97
C4	292-LEU	CD2	4.07
C6	292-LEU	CD2	3.75
C8	292-LEU	CD2	3.67
C10	292-LEU	CD2	3.92
BR2	299-ILE	CD1	3.68
C8	381-HIS	CD2	3.92
C10	381-HIS	CD2	3.78
01	381-HIS	GD2	3.50
01	381-HIS	CE1	3.62
C8	381-HIS	NE2	3.36
C10	381-HIS	NE2	3.34
01	381-HIS	NE2	2.62
C8	401-PHE	CE1	4.02
01	401-PHE	CE1	3.19
C16	401-PHE	CZ	4.03
01	401-PHE	CZ	3.06
03	502-H <sub>2</sub> O	01	3.40

IpBR <sub>2</sub> Atom	Amino Acid	Amino Acid	Distance
•	in full length α	Atom	Å
N1	502-H20	01	3.12
04	503-H <sub>2</sub> O	01	3.20
C17	503-H20	01	3.04
03	503-H <sub>2</sub> O	01	2.27
C15	504-H20	01	4.01
C17	504-H <sub>2</sub> O	01	2.99
03	504-H2O	01	3.80
04	504-H <sub>2</sub> O	01	1.78

Legend to Table 10. The table lists the interactions with IpBr2. The column headings are as follows:

- #1 The atom of IpBr2 that interacts with the amino acid of the receptor. These are also numbered in Figure 32.
  - #2 The amino acid in the full length  $rTR\alpha$  that interacts with the ligand.
  - #3 The name of the atom in the amino acid (standard nomenclature) where the interaction occurs.
  - #4 The distance in Å between IpBr2 and the protein atom.

Table 11

	Table 11			
T3 Atom	Amino Acid	Amino Acid	<u>Distance</u>	
	in full length α	Atom	Å	
12	215-PHE	CD1	4.08	
I1	218-PHE	0	3.19	
I1	218-PHE	CB	3.99	
C4	218-PHE	CB	4.04	
I1	218-PHE	С	3.79	
I1	218-PHE	CB	3.99	
I1	221-ILE	CG1	4.01	
I1	222-ILE	CB	3.95	
	222-ILE	CG1	3.91	
C8	222-ILE	CD1	3.99	
C10	222-ILE	CD1	3.57	
C12	222-ILE	CD1	3.68	
C13	225-ALA	CB	3.66	
C3	225-ALA	СВ	4.04	
04	228-ARG	NH1	3.23	
04	228-ARG	CZ	3.45	
C15	228-ARG	NH2	3.54	
03	228-ARG	NH2	3.90	
04	228-ARG	NH2	2.86	
C10	256-MET	SD	3.73	
C12	256-MET	SD	3.90	
C10	256-MET	CE	3.97	
C12	256-MET	CE	3.92	
	256-MET	CE	3.89	
C11	259-MET	С	3.95	
C11	259-MET	0	3.59	
C14	259-MET	0	3.51	
N1	259-MET	0	3.88	
C1	259-MET	СВ	4.06	
C11	259-MET	СВ	3.77	
C13	259-MET	CB	3.96	
C15	262-ARG	СВ	3.61	
C14	262-ARG	СВ	4.02	
03	262-ARG	CB	3.65	
04	262-ARG	CB	3.92	
04	262-ARG	CD	3.72	
N1	263-ALA	N	3.81	
N1	263-ALA	CA	3.81	
N1	263-ALA	CB	3.63	
N1	275-THR	О	3.54	
	275-THK 276-LEU	CA	3.38	
N1	276-LEU 276-LEU	CA	3.73	
N1		CD1	4.00	
C5	276-LEU	CDI	4.00	

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3.10
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Legend to Table 11. The table lists the interactions with T3. The column headings are as follows:

#1 The atom of T3 that interacts with the amino acid of the receptor. These are also numbered in Figure 32.

- #2 The amino acid in the full length rTRα that interacts with the ligand.
- #3 The name of the atom in the amino acid (standard nomenclature) where the 5 interaction occurs.
  - #4 The distance in Å between T3 and the protein atom.

Table 12

Triac	Amino Acid	Amino Acid	
Atom	in full length hTR β	Atom	Distance Å
I2	269-PHE	CD1	3.75
I2	269-PHE	CE1	3.88
I1	272-PHE	С	4.03
I1	272-PHE	O	3.54
I1	275-ILE	CG1	3.93
I1	276-ILE	CG1	4.02
C3	279-ALA	CB	3.81
C13	279-ALA	CB	3.87
C10	310-MET	SD	3.72
C12	310-MET	SD	3.78
C10	310-MET	CE	4.02
C12	310-MET	CE	3.92
I3	310-MET	CE	3.93
C13	313-MET	CA	3.94
C11	313-MET	C	3.72
C1	313-MET	0	3.79
C11	313-MET	0	3.12
C13	313-MET	0	3.55
C1	313-MET	CB	4.00
C11	313-MET	CB	3.82
C13	313-MET	CB	3.76
C13	313-MET	CG	3.88
O3	316-ARG	CB	3.99
O4	317-ALA	CA	4.08
04	317-ALA	CA	4.10
C11	317-ALA	CB	3.70
I3	317-ALA	CB	4.10
O4	317-ALA	СВ	4.06
O4	320-ARG	NH1	3.58
03	320-ARG	NH2	3.55
04	320-ARG	NH2	4.04
04	329-THR	О	3.55
04	330-LEU	CA	3.42
04	330-LEU	C	3.77
C3	330-LEU	CB	4.06
C5	330-LEU	СВ	4.08
Cl	330-LEU	CD2	4.07
C3	330-LEU	CD2	4.00
C5	330-LEU	CD2	3.73
C7	330-LEU	CD2	3.51
<u>C9</u>	330-LEU	CD2	3.54
C11	330-LEU	CD2	3.86

Triac	Amino Acid	Amino Acid	
Atom	in full length hTR β	Atom	Distance Å
C15	331-ASN	N	3.55
O3	331-ASN	N	3.74
O4	331-ASN	N	3.12
03	331-ASN	CA	4.02
I2	344-GLY	O	3.87
C6	346-LEU	CD2	3.87
C8	346-LEU	CD2	3.84
01	346-LEU	CD2	3.91
I3	353-ILE	CD1	3.51
C8	435-HIS	CD2	3.93
C10	435-HIS	CD2	3.79
01	435-HIS	CD2	3.33
01	435-HIS	CE1	3.81
C8	435-HIS	NE2	3.42
C10	435-HIS	NE2	3.33
01	435-HIS	NE2	2.67
01	442-MET	SD	3.96
01	442-MET	CE	3.72
I2	442-MET	SD	4.01
O1	455-PHE	CE1	3.92
01	455-PHE	CZ	3.50

Legend to Table 12. The table lists the interactions with Triac. The column headings are as follows:

<sup>#1</sup> The atom of Triac that interacts with the amino acid of the receptor. These are also 5 numbered in Figure 32.

<sup>#2</sup> The amino acid in the full length hTR $\beta$  that interacts with the ligand.

<sup>#3</sup> The name of the atom in the amino acid (standard nomenclature) where the interaction occurs.

<sup>#4</sup> The distance in Å between Triac and the protein atom.

Table 13

GC1	Amino Acid	Amino Acid	
Atom	in full length TR β	Atom	Distance Å
C16	269-PHE	CE1	3.99
C19	272-PHE	O	3.85
C16	272-PHE	СВ	3.98
C16	273-THR	CG2	3.76
C19	275-ILE	CG1	3.98
C19	276-ILE	CA	3.98
C2	276-ILE	CD1	3.88
C8	276-ILE	CD1	3.77
C10	276-ILE	CD1	3.58
C12	276-ILE	CD1	3.62
C19	276-ILE	CD1	3.56
C1	279-ALA	СВ	3.68
C3	279-ALA	CB	3.56
O5	279-ALA	CB	3.11
O4	279-ALA	СВ	3.90
O3	282-ARG	CZ	3.53
C17	282-ARG	NH1	3.87
O3	282-ARG	NH1	3.20
O4	282-ARG	NH1	3.85
C17	282-ARG	NH2	3.63
O3	282-ARG	NH2	3.00
C10	310-MET	SD	3.86
C12	310-MET	SD	3.91
C11	313-MET	С	3.85
C11	313-MET	0	3.41
C15	313-MET	0	3.87
C20	313-MET	0	3.99
C11	313-MET	СВ	3.79
C1	313-MET	CG	3.94
C11	313-MET	CG	3.91
O5	313-MET	CG	3.87
O4	313-MET	CG	3.79
C20	314-SER	CA	4.00
C17	316-ARG	CB	3.95
C17	316-ARG	CD	3.80
O3	316-ARG	CD	3.83
O4	316-ARG	CD	3.51
C20	317-ALA	СВ	3.93
C7	330-LEU	CD2	3.56
C9	330-LEU	CD2	3.63
C21	330-LEU	CD2	3.90
O5	331-ASN	N	3.62

GC1 Atom	Amino Acid in full length TR β	Amino Acid Atom	Distance Å
C15	331-ASN	N	3.67
C18	344-GLY	O	3.60
C18	346-LEU	CG	3.89
C6	346-LEU	CD2	3.77
C8	346-LEU	CD2	3.80
C10	435-HIS	CD2	3.89
O1	435-HIS	CD2	3.64
O1	435-HIS	CE1	3.79
C8	435-HIS	NE2	3.44
C10	435-HIS	NE2	3.33
01	435-HIS	NE2	2.77
O1	455-PHE	CE1	3.40
01	455-PHE	CZ	3.22

Legend to Table 13. The table lists the interactions with GC1. The column headings are as follows:

<sup>#1</sup> The atom of GC1 that interacts with the amino acid of the receptor. These are also 5 numbered in Figure 32.

<sup>#2</sup> The amino acid in the full length  $hTR\beta$  that interacts with the ligand.

<sup>#3</sup> The name of the atom in the amino acid (standard nomenclature) where the interaction occurs.

<sup>#4</sup> The distance in Å between GC1 and the protein atom.

AA SS AA SS AA	R <sub>1</sub> -CH <sub>2</sub> -CH(NH <sub>2</sub> )(CO <sub>2</sub> )H	R <sub>2</sub>	R <sub>3</sub>	R <sub>5</sub>	R <sub>6</sub>	R'2	R'3	R' <sub>4</sub>	Ř'5	R' <sub>6</sub>	
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55	ПЭ			<b></b>	1				256	256	
AA SS			<del> </del>	-						H5-H6	<del></del>
	259			+	259		<del> </del>		113-110	113-110	
AA	H5-H6		-	<del> </del>	H5-H6						
SS	262			<del> </del>	H3-H0		<del></del>				
AA SS	H5-H6				<del> </del>		<del> </del>				
				<del> </del>	<del> </del>			<del> </del>			
AA	263 H5-H6		_	ļ	ļ			ļ	<u> </u>		ļ
SS				ļ			<del> </del>	<del> </del>	ļ		<u> </u>
AA	266				<del> </del>			<u> </u>	<del> </del>		
SS	loop		_	<u> </u>	ļ	<u> </u>				<del></del>	<del> </del>
AA	275				<del> </del>	ļ		<del> </del>	<del> </del>		
SS	S3		256	276	076	ļ	ļ	<del> </del>			
AA	276		276	276	276			<del></del>	-	ļ	
SS	S3		S3	S3	S3			ļ	-		ļ
AA	277			1		ļ			<u> </u>		
SS	loop						200 201				-
AA					_	-	290-291	<u> </u>		ļ	<del> </del>
SS						200	loop	1 200	202		292
AA						292		292	292	<del> </del>	
SS				505		loop	loop	loop	loop		loop
AA				299				ļ		ļ	-
SS				Н8				1 201	201		<del></del>
AA						-	<b>_</b>	381	381	<u> </u>	<del> </del>
SS						ļ		H11	H11	ļ	<del> </del>
AA						<u> </u>	388			-	<del> </del>
SS							H11	<u> </u>			<del> </del>
AA							401	401			<u> </u>
SS							H12	H12	<u> </u>		<del> </del>
AA	HOH502/HOH503 /HOH504										

AA = Amino Acid

SS = Secondary Structure

	Coordination Structure of											
Coordination Structure	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>	R <sub>5</sub>	R <sub>6</sub>	R'2	R'3	R' <sub>4</sub>	R'5	R'6	Х	
Structure	-CH <sub>2</sub> -COOH	-H	-I	-I	-H	-H	-Ī	-OH	-H	-H	0	
AA			218									
SS	-		H3									
AA			221									
SS			H3									
AA							222	222	222	222		
SS							H3	H3	H3	H3		
AA	225		7									
SS	H3											
AA				256					256	256		
SS				H5-H6					H5-H6	H5-H6		
AA	259	<u> </u>			259							
SS	H5-H6				H5-H6							
AA	262											
SS	H5-H6											
AA	263											
SS	H5-H6											
AA	266										<u> </u>	
SS	loop											
AA	275											
SS	S3											
AA	276		276	276	276							
SS	S3		S3	S3	S3							
AA	277											
SS	loop											
AA							290					
SS							loop					
AA		İ				292	292	292	292		292	
SS						loop	loop	loop	loop		loop	
AA				299								
SS				H8								
AA								381	381			
SS								H11	H11			
AA								388				
SS								H11				
AA							401	401				
SS							H12	H12				

5 AA = Amino Acid SS = Secondary Structure

Table 16
Coordination Structure of TR-α and IpBr2

Coordina-	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>	R <sub>5</sub>	R <sub>6</sub>	R'2	R'3	R'4	R'5	R' <sub>6</sub>	X
tion		-			-				İ		
Structure										ŀ	1
	-CH <sub>2</sub> -CH(NH <sub>2</sub> )(CO <sub>2</sub> )H	-H	-Br	-Br	-H	-H	-CH(CH <sub>3</sub> ) <sub>2</sub>	-OH	-H	-H	O
AA	1						215				
SS					-,		Н3				
AA			218				218				
SS			H3				Н3				
AA							219				
SS							НЗ				
AA			221								
SS			H3								
AA							222	222	222	222	
SS							H3	H3	Н3	Н3	
AA	225										
SS	H3										
AA	228										
SS	H3										
AA	-				256				256	256	
SS					H5-H6				H5-H6	H5-H6	
AA	259				259						
SS	H5-H6	1			H5-H6						
AA	262										
SS	H5-H6	1									
AA	263		1								
SS	H5-H6										
AA	266										
SS	loop										
AA	275										
SS	S3										
AA	276		276	276	276						
SS	S3		S3	S3	S3	1					
ĀA	277										
SS				ļ						ļ	
AA							290-291				
SS							loop			ļ	ļ
AA						292	292	292	292		292
SS						loop	loop	loop	loop		loop
AA				299							1
SS				H8							
AA								381	381		1
SS								HII	H11		
AA							401	401			
SS							H12	H12			
AA	HOH502/HOH503/ HOH504								ļ		ļ
SS				CC -	C1-	CAm					

AA = Amino Acid

SS = Secondary Structure

Coordination	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>	R <sub>5</sub>	R <sub>6</sub>	R'2	R'3	R' <sub>4</sub>	R'5	R'6	Х
Structure			<u> </u>					OII	-H	-H	0
	-CH <sub>2</sub> -CH(NH <sub>2</sub> )(CO <sub>2</sub> )H	-H	-I	-I	-H	-H	-I	-OH	-H	-H	
AA							215				
SS						210	НЗ				
AA			218			218					
SS	-		H3			Н3		-			
AA			221								
SS			H3				200	000	222	222	
AA							222	222	222 H3		
SS							Н3	Н3	H3	Н3	
AA	225		<u> </u>								<del> </del>
SS	H3										<del> </del>
AA	228			ļ							
SS	H3								256	256	<del></del>
AA					256				256	256	
SS					H5-H6			<u> </u>	H5-H6	H5-H6	
AA	259				259						
SS	H5-H6				H5-H6						
AA	262						ļ	<u> </u>			
SS	H5-H6							ļ			
AA	263			ļ							<u> </u>
SS	Н5-Н6	1						ļ			ļ
AA	275			<u> </u>							
SS	S3			<u> </u>							<u> </u>
AA	276		276	276	276			ļ			<del> </del>
SS	S3		S3	S3	S3			<u> </u>		<u> </u>	<u> </u>
AA	277							ļ	ļ		
SS		<u> </u>							ļ		<del> </del>
AA							290	<u> </u>			ļ
SS							loop	1			
AA		<u> </u>				292	292	292	292		292
SS						loop	loop	loop	loop	ļ	loop
AA				299		<u> </u>			ļ	<del> </del>	<b></b>
SS		<u> </u>		H8		ļ <u>.</u>		1001	1 201		
AA							ļ	381	381		
SS							1	H11	H11		
AA							1	388		-	
SS							1	H11	1		
AA							401	401		1	
SS							H12	H12		-	
AA	HOH502/H0H503/ HOH504										
SS	4 :1 66 6		1 0								

AA = Amino Acid SS = Secondary Structure

Table 18 Coordination Structure of TR- $\beta$  and Triac

				Struct							<del></del>
Coordination	R1	R2	R3	R5	R6	R2'	R3	R4	R5	R6	X
Structure										<del></del>	
	-CH <sub>2</sub> CO <sub>2</sub> H	Н	I	I	Н	Н	I	ОН	Н	Н	0
AA							269				
SS							Н3				
AA			272								
SS			H3								ļ
AA			275								
SS			H3								
AA			276								
SS			Н3								
AA	279	279									
SS	Н3	H3									<u> </u>
AA				310					310	310	
SS				H5-H6					H5-H6	H5-H6	
AA	313				313						
SS	H5-H6				H5-H6	1					
AA	316										
SS	H5-H6										ļ
AA	317				317		317				
SS	H5-H6				H5-H6		H5-H6				<u> </u>
AA	320										
SS	H5-H6					T					
AA	329										<u> </u>
SS	S3										
AA	330	330	330	330	330						
SS	S3	S3	S3	S3	S3						
AA	331										
SS	loop										
AA							344				ļ
SS							loop				
AA							346	346			
SS	-					T	loop	loop			
AA		1		353							
SS				H8							
AA								435	435		
SS	1	1						H11	H11		
AA		T	1				442	442			
SS				1			H11	H11			
AA	-							455			
SS			"					H12			

AA = Amino Acid SS = Secondary Structure

Table 19
Coordination Structure of TR-β and GC1

Coordination Structure of TR-B and GC1													
Coordina-	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>	R <sub>5</sub>	R <sub>6</sub>	R2	R3	R4	R5	R6	Х		
tion													
Structure											ATT		
	-O-CH <sub>2</sub> CO <sub>2</sub> H	Н	CH <sub>3</sub>	CH <sub>3</sub>	Н	H	CH(CH <sub>3</sub> )	ОН	H	Н	CH <sub>2</sub>		
AA							269						
SS							Н3						
AA			272										
SS			Н3		,								
AA			273				273				<u> </u>		
SS			Н3				Н3						
AA			275				ļ				<u> </u>		
SS			H3					276	276	276	<u> </u>		
AA		<u> </u>	276					276	276 H3	276 H3			
SS			Н3					НЗ	нэ	H3	<u> </u>		
AA	279	279	ļ							<u> </u>	<u> </u>		
SS	H3	НЗ								-	<del> </del>		
AA SS	282		ļ				-				<u> </u>		
	Н3					<u></u>			210	310	<del> </del>		
AA			1	310	ļ		ļ		310		<del>                                     </del>		
SS				Н5-Н6					H5- H6	Н5-Н6			
AA	313				313								
SS	H5-H6				H5-H6								
AA							314						
SS						<u> </u>	H5-H6						
AA	316										ļ		
SS	H5-H6				<u> </u>		_				ļ		
AA							317				ļ		
SS							H5-H6				<u> </u>		
AA	320							ļ	ļ		4		
SS	Н5-Н6					<u> </u>				ļ	-		
AA	329					<u> </u>		ļ		ļ	<del></del>		
SS	S3		<u> </u>								<del> </del>		
AA	330	<u> </u>		330	-	ļ		<del> </del>	ļ	-	+		
SS	S3	1	1	S3	ļ	ļ			ļ		<del> </del>		
AA	331		4	<del> </del>		-			-	<del> </del>	+		
SS	loop				-	-	- 244	ļ	<b> </b>		+		
AA						-	344		ļ		<del> </del>		
SS		ļ				+	loop	346			+		
AA		_		ļ			346		<del> </del>	-	+-		
SS				1 252		<del> </del>	loop	loop			+-		
AA				353		-		-	-	<del> </del>	+		
SS			_	H8				435	435	<del> </del>			
AA													
	_							H11 455	H11	-	+-		
		<b>.</b>		<u> </u>		-			ļ	-	+		
SS								H12					

AA = Amino Acid

SS = Secondary Structure

## **APPENDIX 3**

## TR\_DMT.PDB

REMARK TR\_dmt full length numbering

REMARK

5 REMARK Rfactor 0.205 Rfree 0.227

REMARK Resolution 15. 2.2 all reflections

**REMARK** 

REMARK Three cacodylate-modified cysteines (CYA)

REMARK Cya334, Cya380, Cya392

10 REMARK cacodylate modeled as single arsenic atom

REMARK

REMARK side chain of certain residues modeled as ALA due to poor density;

REMARK however, residue name reflects true residue for clarity

REMARK

15 REMARK clone obtained from Murray et. al.

REMARK deposited sequence confirmed,

REMARK differing from that reported by Thompson et. al.

REMARK in the following codons:

REMARK 281 Thr - Ala

20 REMARK 285 Lys - Glu

REMARK identical to that reported by Mitsuhashi et. al.

REMARK gb:RNTRAVI X07409

JRNL

45

AUTH

M.B.

MURRAY,

N.D.ZILZ,

N.L.MCCREARY, M.J.MACDONALD

25 JRNL AUTH 2 H.C.TOWLE

JRNL TITL ISOLATION AND CHARACTERIZATION OF RAT CDNA CLONES FOR TWO

JRNL TITL 2 DISTINCT THYROID HORMONE RECPTORS

JRNL REF JBC

V. 263 25 1988

JRNL AUTH C.C.THOMPSON, C.WEINBERGER, R.LEBO, R.M.EVANS JRNL TITL IDENTIFICATION OF A NOVEL THYROID HORMONE RECEPTOR EXPRESSED

JRNL TITL 2 IN THE MAMMALIAN CENTRAL NERVOUS SYSTEM

JRNL REF SCIENCE

V. 237 1987

35 JRNL AUTH T.MITSUHASHI,G.TENNYSON,V.NIKODEM

JRNL TITL NUCLEOTIDE SEQUENCE OF NOVEL CDNAS GENERATED BY ALTERNATIVE

JRNL TITL 2 SPLICING OF A RAT THYROID HORMONE RECEPTOR GENE TRANSCRIPT

40 JRNL REF NUC. ACIDS. RES. V. 16 12 1988

ATOM 1 N ARG 157 68.504 8.445 5.651 1.00 68.93

ATOM 2 CA ARG 157 67.886 9.543 6.398 1.00 56.98

ATOM 3 CB ARG 157 68.769 10.789 6.324 1.00 59.25

ATOM 4 CG ARG 157 70.147 10.632 6.932 1.00 58.90

ATOM 5 CD ARG 157 70.068 10.422 8.425 1.00 59.37

ATOM 6 NE ARG 157 71.392 10.446 9.036 1.00 63.94

ATOM 7 CZ ARG 157 71.613 10.329 10.341 1.00 64.39

ATOM 8 NH1 ARG 157 70.596 10.182 11.179 1.00 62.14

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72.855 10.365 10.808 1.00 65.56
             9 NH2 ARG 157
    ATOM
                              66.500 9.881 5.854 1.00 48.97
             10 C ARG 157
    ATOM
                              66.351 10.203 4.674 1.00 48.61
             11 O ARG 157
    ATOM
                              65.469 9.818 6.712 1.00 41.90
    ATOM
             12 N PRO 158
                               65.550 9.366 8.112 1.00 41.06
             13 CD PRO 158
5
    ATOM
                               64.083 10.114 6.333 1.00 39.34
             14 CA PRO 158
    ATOM
                               63.286 9.704 7.576 1.00 37.89
             15 CB PRO 158
    ATOM
                               64.260 9.883 8.693 1.00 42.40
             16 CG PRO 158
    ATOM
             17 C PRO 158
                              63.814 11.573 5.930 1.00 37.10
    ATOM
                              64.189 12.517 6.636 1.00 33.31
             18 O PRO 158
10
    ATOM
                              63.171 11.733 4.778 1.00 30.56
             19 N GLU 159
    ATOM
                               62.821 13.038 4.231 1.00 24.26
             20 CA GLU 159
    ATOM
                               62.553 12.904 2.727 1.00 19.19
             21 CB GLU 159
    ATOM
                               63.788 12.677 1.874 1.00 20.60
             22 CG GLU 159
    ATOM
                               64.407 13.971 1.390 1.00 26.54
             23 CD GLU 159
    ATOM
15
                               63.649 14.929 1.115 1.00 30.85
             24 OE1 GLU 159
    ATOM
                               65.649 14.027 1.268 1.00 28.35
             25 OE2 GLU 159
    ATOM
                              61.549 13.520 4.909 1.00 23.26
             26 C GLU 159
    ATOM
                               60.906 12.765 5.643 1.00 26.86
             27 O GLU 159
    ATOM
                              61.200 14.806 4.729 1.00 22.72
             28 N PRO 160
20
    ATOM
                               61.981 15.916 4.153 1.00 17.87
             29 CD PRO 160
     ATOM
                               59.969 15.292 5.359 1.00 19.90
             30 CA PRO 160
    ATOM
             31 CB PRO 160
                               60.004 16.799 5.070 1.00 14.42
    ATOM
                               61.465 17.109 4.919 1.00 12.87
             32 CG PRO 160
    ATOM
                              58.747 14.623 4.701 1.00 23.68
             33 C PRO 160
25
    ATOM
                              58.730 14.383 3.491 1.00 24.72
     ATOM
             34 O PRO 160
             35 N THR 161
                               57.749 14.281 5.506 1.00 22.19
     ATOM
                               56.542 13.660 4.985 1.00 19.50
             36 CA THR 161
     ATOM
             37 CB THR 161
                               55.691 13.031 6.125 1.00 21.50
     ATOM
                                55.163 14.062 6.972 1.00 20.33
             38 OG1 THR 161
30
     ATOM
                                56.537 12.078 6.959 1.00 19.48
             39 CG2 THR 161
     ATOM
                               55.744 14.765 4.298 1.00 22.86
             40 C THR 161
     ATOM
                               56.040 15.949 4.481 1.00 27.68
     ATOM
             41 O THR 161
                               54.720 14.403 3.504 1.00 20.36
             42 N PRO 162
     ATOM
                               54.280 13.050 3.113 1.00 16.55
             43 CD PRO 162
35
     ATOM
                               53.924 15.435 2.830 1.00 21.97
     ATOM
             44 CA PRO 162
                               52.780 14.633 2.210 1.00 18.17
             45 CB PRO 162
     ATOM
                               53.422 13.316 1.905 1.00 18.01
     ATOM
             46 CG PRO 162
             47 C PRO 162
                               53.399 16.467 3.826 1.00 22.56
     ATOM
                               53.461 17.675 3.567 1.00 21.73
             48 O PRO 162
     ATOM
40
                               52.912 15.976 4.967 1.00 25.28
     ATOM
             49 N GLU 163
                                52.357 16.816 6.030 1.00 26.64
             50 CA GLU 163
     ATOM
                                51.743 15.962 7.144 1.00 30.22
             51 CB GLU 163
     ATOM
                                50.514 15.131 6.748 1.00 44.99
             52 CG GLU 163
     ATOM
                                50.836 13.950 5.831 1.00 48.88
             53 CD GLU 163
45
     ATOM
                                50.016 13.660 4.929 1.00 52.48
     ATOM
             54 OE1 GLU 163
                                51.895 13.309 6.015 1.00 44.23
             55 OE2 GLU 163
     ATOM
                               53.414 17.731 6.634 1.00 27.65
     ATOM
             56 C GLU 163
                               53.114 18.862 7.034 1.00 29.30
             57 O GLU 163
     ATOM
                               54.646 17.235 6.712 1.00 21.89
             58 N GLU 164
     ATOM
50
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```
55.741 18.015 7.265 1.00 18.29
             59 CA GLU 164
    ATOM
                               56.901 17.109 7.657 1.00 14.78
             60 CB GLU 164
    ATOM
                               56.552 16.196 8.825 1.00 21.11
             61 CG GLU 164
    ATOM
                               57.669 15.249 9.198 1.00 20.35
             62 CD GLU 164
    ATOM
             63 OE1 GLU 164
                                58.605 15.071 8.392 1.00 28.55
    ATOM
                                57.610 14.677 10.302 1.00 28.25
             64 OE2 GLU 164
    ATOM
                               56.200 19.097 6.306 1.00 24.62
    ATOM
             65 C GLU 164
                               56.574 20.183 6.741 1.00 32.05
             66 O GLU 164
    ATOM
                              56.174 18.817 5.003 1.00 28.22
             67 N TRP 165
    ATOM
             68 CA TRP 165
                               56.576 19.825 4.021 1.00 22.99
10
    ATOM
                               56.575 19.262 2.605 1.00 17.37
    ATOM
             69 CB TRP 165
                               57.876 18.633 2.210 1.00 10.74
    ATOM
             70 CG TRP 165
                               59.153 19.283 2.109 1.00 11.74
    ATOM
             71 CD2 TRP
                         165
                               60.075 18.319 1.648 1.00 9.97
             72 CE2 TRP
                         165
    ATOM
                               59.606 20.583 2.365 1.00 13.88
             73 CE3 TRP 165
    ATOM
15
                                58.074 17.343 1.832 1.00 9.17
             74 CD1 TRP 165
    ATOM
                                59.390 17.145 1.486 1.00 16.55
             75 NE1 TRP 165
    ATOM
                               61.427 18.613 1.436 1.00 13.37
    ATOM
             76 CZ2 TRP 165
                               60.954 20.874 2.156 1.00 16.15
             77 CZ3 TRP 165
     ATOM
                                61.846 19.892 1.696 1.00 17.42
20
     ATOM
             78 CH2 TRP 165
             79 C TRP 165
                              55.634 21.015 4.115 1.00 21.44
     ATOM
                               56.041 22.149 3.865 1.00 22.12
    ATOM
             80 O TRP 165
                               54.373 20.747 4.456 1.00 21.29
     ATOM
             81 N ASP 166
             82 CA ASP 166
                               53.369 21.796 4.621 1.00 25.77
     ATOM
                               51.972 21.196 4.808 1.00 26.02
             83 CB ASP 166
25
     ATOM
                               51.428 20.559 3.539 1.00 33.01
             84 CG ASP 166
     ATOM
                                51.874 20.932 2.434 1.00 29.48
             85 OD1 ASP 166
     ATOM
                                50.537 19.692 3.649 1.00 34.47
             86 OD2 ASP 166
     ATOM
                              53.732 22.637 5.842 1.00 27.91
             87 C ASP 166
     ATOM
                               53.744 23.865 5.767 1.00 31.28
     ATOM
             88 O ASP 166
30
                               54.046 21.966 6.951 1.00 25.57
     ATOM
             89 N LEU 167
                               54.439 22.640 8.187 1.00 28.28
             90 CA LEU 167
     ATOM
                               54.854 21.624 9.256 1.00 32.80
             91 CB LEU 167
     ATOM
                                53.945 21.347 10.455 1.00 41.75
             92 CG LEU 167
     ATOM
                                54.765 20.640 11.532 1.00 39.15
             93 CD1 LEU 167
     ATOM
35
                                53.374 22.647 11.008 1.00 39.20
     ATOM
             94 CD2 LEU 167
             95 C LEU 167
                               55.636 23.532 7.902 1.00 22.19
     ATOM
                               55.671 24.700 8.302 1.00 29.51
             96 O LEU 167
     ATOM
                              56.610 22.957 7.206 1.00 15.01
             97 N ILE 168
     ATOM
40
             98 CA ILE 168
                               57.846 23.632 6.833 1.00 18.03
     ATOM
                               58.756 22.668 6.040 1.00 11.37
             99 CB ILE 168
     ATOM
                                59.890 23.413 5.367 1.00 16.36
             100 CG2 ILE 168
     ATOM
                                59.289 21.580 6.975 1.00 21.63
     ATOM
             101 CG1 ILE 168
                                60.095 20.501 6.287 1.00 21.03
     ATOM
             102 CD1 ILE 168
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             103 C ILE 168
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                               58.155 25.948 6.300 1.00 24.88
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             104 O ILE 168
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                               56.337 25.934 4.190 1.00 21.28
             106 CA HIS 169
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                               55.411 25.493 3.057 1.00 22.29
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             107 CB HIS
                         169
                               56.047 24.543 2.091 1.00 23.11
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             108 CG HIS 169
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                               56.130 22.974 0.546 1.00 15.89
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            111 CE1 HIS 169
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            112 NE2 HIS 169
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                              56.033 28.215 4.842 1.00 21.53
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                               54.679 26.685 5.795 1.00 17.13
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            115 N VAL 170
                                53.957 27.661 6.607 1.00 21.29
            116 CA VAL 170
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                                52.808 26.991 7.399 1.00 24.33
            117 CB VAL 170
     ATOM
            118 CG1 VAL 170
                                52.164 27.985 8.354 1.00 23.78
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                                51.760 26.439 6.435 1.00 18.87
            119 CG2 VAL 170
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                               54.910 28.382 7.567 1.00 24.69
            120 C VAL 170
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                               54.912 29.616 7.637 1.00 28.77
            121 O VAL 170
     ATOM
                               55.759 27.609 8.245 1.00 20.35
            122 N ALA 171
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                                56.722 28.148 9.202 1.00 19.61
            123 CA ALA 171
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            124 CB ALA 171
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                               57.775 29.026 8.531 1.00 20.91
            125 C ALA 171
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                               58.102 30.105 9.041 1.00 21.98
            126 O ALA 171
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                               58.308 28.571 7.398 1.00 18.94
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                                59.313 29.342 6.668 1.00 19.55
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            128 CA THR 172
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            129 CB THR 172
                                60.394 27.336 5.795 1.00 20.66
            130 OG1 THR 172
     ATOM
                                60.894 29.418 4.702 1.00 20.44
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            131 CG2 THR 172
            132 C THR 172
                               58.730 30.697 6.254 1.00 23.26
     ATOM
                               59.403 31.724 6.334 1.00 24.32
            133 O THR 172
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     ATOM
                               57.468 30.694 5.836 1.00 27.42
            134 N GLU 173
     ATOM
                                56.797 31.922 5.434 1.00 27.68
            135 CA GLU 173
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                                55.477 31.605 4.728 1.00 24.51
     ATOM
            136 CB GLU 173
            137 CG GLU 173
                                54.652 32.836 4.338 1.00 39.69
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                                55.396 33.814 3.426 1.00 47.72
            138 CD GLU 173
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                                55.019 35.009 3.417 1.00 48.26
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            139 OE1 GLU 173
                                56.344 33.398 2.717 1.00 49.61
            140 OE2 GLU 173
     ATOM
                               56.557 32.834 6.641 1.00 25.68
            141 C GLU 173
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                               56.773 34.046 6.559 1.00 23.39
             142 O GLU 173
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            143 N ALA 174
                               56.119 32.245 7.755 1.00 25.19
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                                55.863 32.989 8.993 1.00 22.25
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             144 CA ALA 174
            145 CB ALA 174
                                55.450 32.030 10.111 1.00 15.95
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                               57.125 33.747 9.391 1.00 23.22
            146 C ALA 174
     ATOM
                               57.076 34.918 9.768 1.00 24.52
             147 O ALA 174
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                               58.261 33.073 9.275 1.00 20.97
            148 N HIS 175
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     ATOM
                               59.544 33.665 9.606 1.00 19.55
             149 CA HIS 175
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                               60.625 32.577 9.649 1.00 16.19
            150 CB HIS 175
     ATOM
                               62.016 33.104 9.835 1.00 18.89
            151 CG HIS 175
     ATOM
                                63.148 32.901 9.119 1.00 16.05
             152 CD2 HIS 175
     ATOM
             153 ND1 HIS 175
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     ATOM
                                63.642 34.265 10.765 1.00 15.87
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             154 CE1 HIS 175
                                64.143 33.635 9.718 1.00 19.19
             155 NE2 HIS 175
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                               59.934 34.757 8.617 1.00 21.28
             156 C HIS 175
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                               60.274 35.869 9.014 1.00 25.12
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             157 O HIS 175
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             158 N ARG 176
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            159 CA ARG 176
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                                61.286 33.795 4.602 1.00 43.20
            161 CG ARG 176
    ATOM
                                61.197 33.334 3.170 1.00 50.07
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            162 CD ARG 176
                                62.316 32.477 2.813 1.00 58.20
            163 NE ARG 176
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                                62.266 31.548 1.867 1.00 67.22
            164 CZ ARG 176
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                                61.143 31.358 1.182 1.00 67.62
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            165 NH1 ARG 176
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            166 NH2 ARG 176
            167 C ARG 176
                               59.487 36.688 6.325 1.00 23.97
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            168 O ARG 176
                               60.073 37.760 6.209 1.00 24.52
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                              58.177 36.598 6.515 1.00 23.60
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                               57.341 37.789 6.565 1.00 26.36
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            170 CA SER 177
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                               55.495 36.459 7.423 1.00 25.97
            172 OG SER 177
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                              57,557 38,623 7,829 1,00 28,76
            173 C SER 177
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            174 O SER 177
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                               58.257 38.062 8.815 1.00 25.52
            175 N THR 178
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                               58.508 38.772 10.064 1.00 18.93
            176 CA THR 178
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                               57.828 38.064 11.258 1.00 21.81
            177 CB THR 178
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                                58.348 36.736 11.394 1.00 24.18
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            178 OG1 THR 178
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            179 CG2 THR 178
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                               59.993 38.967 10.358 1.00 20.69
            180 C THR 178
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    ATOM
            181 O THR 178
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                               60.837 38.645 9.385 1.00 23.68
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                               62.275 38.802 9.555 1.00 28.22
            183 CA ASN 179
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            184 CB ASN 179
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            185 CG ASN 179
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            186 OD1 ASN 179
            187 ND2 ASN 179
                                64.702 37.865 10.667 1.00 31.14
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            188 C ASN 179
                               62.689 40.115 8.902 1.00 34.47
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                               62.832 40.200 7.678 1.00 36.54
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            189 O ASN 179
                               62.874 41.135 9.735 1.00 37.39
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                                63.235 42.479 9.292 1.00 33.71
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            191 CA ALA 180
            192 CB ALA 180
                                63.555 43.352 10.494 1.00 31.57
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                               64.375 42.545 8.284 1.00 37.87
            193 C ALA 180
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                               65.458 42.018 8.525 1.00 35.26
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            195 N GLN 181
                               64.095 43.187 7.150 1.00 40.55
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                                65.049 43.391 6.057 1.00 42.95
            196 CA GLN 181
    ATOM
            197 CB GLN 181
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    ATOM
            198 CG GLN 181
                                66.144 45.326 7.383 1.00 52.70
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            199 CD GLN 181
                                65.351 46.399 6.650 1.00 55.03
    ATOM
                                65.270 46.412 5.421 1.00 59.56
            200 OE1 GLN 181
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                                64.757 47.308 7.411 1.00 54.39
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            201 NE2 GLN 181
                               65.391 42.176 5.197 1.00 44.27
            202 C GLN 181
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                               66.181 42.291 4.251 1.00 46.47
            203 O GLN 181
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                               64.797 41.025 5.508 1.00 42.17
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            204 N GLY 182
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            205 CA GLY 182
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            211 OG SER 183
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            212 C SER 183
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                              68.223 41.482 2.535 1.00 55.77
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                               68.854 42.775 2.342 1.00 57.78
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           215 CA HIS 184
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           216 C HIS 184
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                              70.312 44.301 3.454 1.00 60.34
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            217 O HIS 184
            218 N TRP 185
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                               70.159 43.020 5.923 1.00 53.73
            219 CA TRP 185
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                               69.973 41.973 7.030 1.00 50.40
            220 CB TRP 185
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                               70.746 40.694 6.837 1.00 48.09
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                                72.091 40.419 7.269 1.00 47.38
            222 CD2 TRP 185
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                               72.390 39.094 6.888 1.00 40.29
            223 CE2 TRP 185
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                               73.071 41.169 7.937 1.00 45.43
            224 CE3 TRP 185
    ATOM
                                70.301 39.554 6.234 1.00 49.87
            225 CD1 TRP 185
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                                71.280 38.589 6.262 1.00 48.02
            226 NE1 TRP 185
    ATOM
                               73.628 38.496 7.154 1.00 38.65
            227 CZ2 TRP 185
    ATOM
                               74.304 40.573 8.201 1.00 43.26
    ATOM
            228 CZ3 TRP 185
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                                74.570 39.250 7.807 1.00 40.00
            229 CH2 TRP 185
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                              71.638 43.386 5.800 1.00 55.99
            230 C TRP 185
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    ATOM
            231 O TRP 185
                               72.089 44.359 6.401 1.00 52.84
                               72.389 42.614 5.021 1.00 59.15
            232 N LYS 186
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                               73.818 42.863 4.843 1.00 64.01
            233 CA LYS 186
25
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                               74.466 41.688 4.091 1.00 64.67
            234 CB LYS 186
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                               75.943 41.868 3.729 1.00 65.58
            235 CG LYS 186
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                               76.817 42.181 4.946 1.00 62.03
     ATOM
            236 CD LYS 186
                               78.238 42.512 4.515 1.00 61.52
            237 CE LYS 186
     ATOM
            238 NZ LYS 186
                               78.988 43.243 5.579 1.00 61.67
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                               74.131 44.203 4.160 1.00 67.49
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            239 C LYS 186
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                               73.221 44.678 3.316 1.00 68.99
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                                73.431 45.939 2.612 1.00 69.65
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                                72.880 45.867 1.180 1.00 73.76
            243 CB GLN 187
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                                73.632 44.935 0.237 1.00 78.61
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            244 CG GLN 187
                                73.368 43.471 0.525 1.00 84.96
            245 CD GLN 187
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                                74.203 42.782 1.109 1.00 87.73
            246 OE1 GLN 187
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            247 NE2 GLN 187
                                72.197 42.989 0.122 1.00 84.98
            248 C GLN 187
                               72.817 47.141 3.323 1.00 69.16
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            249 O GLN 187
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                               71.666 46.936 3.953 1.00 65.82
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                                70.961 48.014 4.639 1.00 65.00
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            251 CA ARG 188
                                69.458 47.739 4.591 1.00 66.20
            252 CB ARG 188
     ATOM
            253 CG ARG 188
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     ATOM
                                67.463 47.212 3.132 1.00 78.59
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            254 CD ARG 188
                                67.003 47.008 1.760 1.00 87.71
            255 NE ARG 188
     ATOM
                                67.011 47.946 0.814 1.00 94.10
            256 CZ ARG 188
     ATOM
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            257 NH1 ARG 188
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            258 NH2 ARG 188
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71.409 48.286 6.077 1.00 65.39
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    ATOM
                               72.372 47.506 6.561 1.00 64.28
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                                72.882 47.654 7.922 1.00 60.75
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                               73.691 46.409 8.321 1.00 56.87
            263 CB ARG 189
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                                75.050 46.308 7.630 1.00 59.52
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           265 CD ARG 189
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                                75.874 44.348 8.907 1.00 55.48
           266 NE ARG 189
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                                77.055 43.849 9.257 1.00 61.38
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            267 CZ ARG 189
            268 NH1 ARG 189
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                               73.747 48.907 8.082 1.00 60.91
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                               74.548 49.245 7.207 1.00 60.67
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                               73.575 49.591 9.207 1.00 59.06
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            273 CA LYS 190
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                               76.304 50.721 10.944 1.00 50.49
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            278 CA PHE 191
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                                79.090 49.423 11.142 1.00 49.66
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            280 CG PHE 191
                                78.873 49.348 9.768 1.00 51.03
            281 CD1 PHE 191
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                                79.845 48.429 11.759 1.00 46.28
            282 CD2 PHE 191
     ATOM
                                79.403 48.298 9.018 1.00 51.35
            283 CE1 PHE 191
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            284 CE2 PHE 191
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                               80.158 47.311 9.646 1.00 48.48
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                               76.663 51.534 13.248 1.00 48.61
            286 C PHE 191
     ATOM
            287 O PHE 191
                               76.507 52.720 12.952 1.00 50.38
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                               76.488 51.068 14.479 1.00 47.31
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            289 CA LEU 192
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                                75.397 51.949 18.068 1.00 31.01
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                               78.528 52.179 15.932 1.00 39.71
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                               77.350 54.104 15.781 1.00 45.15
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             296 N PRO 193
             297 CD PRO 193
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             298 CA PRO 193
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                                76.571 56.308 15.565 1.00 41.66
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                               79.476 54.498 17.028 1.00 43.34
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             302 O PRO 193
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                                81.781 53.804 17.512 1.00 47.20
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                               81.381 55.698 19.025 1.00 55.21
             308 N ASP 195
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            310 CB ASP 195
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                               75.179 56.171 19.541 1.00 45.25
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            329 CA GLN 198
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                                83.232 53.718 23.316 1.00 69.39
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            332 CD GLN 198
                                84.088 52.484 23.483 1.00 76.76
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           333 OE1 GLN 198
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                                85.205 52.632 24.192 1.00 78.09
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                               81.915 53.678 26.922 1.00 57.56
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            340 OG SER 199
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            343 N PRO 200
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             344 CD PRO 200
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            345 CA PRO 200
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             347 CG PRO 200
     ATOM
             348 C PRO 200
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             349 O PRO 200
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             350 N ILE 201
                              78.532 53.241 32.867 1.00 49.57
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                               78.525 53.924 34.158 1.00 49.15
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             351 CA ILE 201
             352 CB ILE 201
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                                78.429 56.150 35.306 1.00 53.37
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             353 CG2 ILE 201
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                                79.137 56.037 32.934 1.00 52.55
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             354 CG1 ILE 201
             355 CD1 ILE 201
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             357 O ILE 201
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            362 CG2 VAL 202
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            364 O VAL 202
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            367 CB SER 203
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                              74.285 48.712 38.544 1.00 57.50
            370 O SER 203
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            371 N MET 204
                               75.923 47.283 37.958 1.00 52.29
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                               75.032 45.487 36.548 1.00 47.74
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            373 CB MET 204
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                               72.491 46.348 35.953 1.00 40.93
            375 SD MET 204
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                               71.947 44.785 35.241 1.00 39.19
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            377 C MET 204
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            380 CD PRO 205
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            381 CA PRO 205
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            383 CG PRO 205
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            385 O PRO 205
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            390 OD1 ASP 206
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            395 CA GLY 207
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                               80.169 44.585 36.482 1.00 51.96
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            397 O GLY 207
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            398 N ASP 208
                               79.510 44.005 35.481 1.00 52.50
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            399 CA ASP 208
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            401 CG ASP 208
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                                81.130 43.006 32.335 1.00 57.42
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            402 OD1 ASP 208
            403 OD2 ASP 208
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            404 C ASP 208
                               78.497 45.823 34.187 1.00 46.68
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                               77.283 45.671 34.332 1.00 45.81
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            406 N LYS 209
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            408 CB LYS 209
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            412 CA VAL 210
           413 CB VAL 210
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                                73.269 49.926 30.937 1.00 27.92
           414 CG1 VAL 210
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                                73.818 48.183 32.627 1.00 29.43
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                               76.090 52.079 32.038 1.00 39.57
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                               76.019 52.544 29.254 1.00 38.39
            419 CA ASP 211
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            420 CB ASP 211
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                               77.051 53.620 27.177 1.00 36.85
            421 CG ASP 211
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            422 OD1 ASP 211
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                                78.121 53.716 26.553 1.00 33.87
            423 OD2 ASP 211
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     ATOM
                              74.601 53.040 28.958 1.00 40.60
            424 C ASP 211
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                              73.919 52.517 28.073 1.00 40.36
     ATOM 425 O ASP 211
                               74.185 54.074 29.680 1.00 41.55
     ATOM 426 N LEU 212
                               72.854 54.664 29.552 1.00 38.39
     ATOM 427 CA LEU 212
     ATOM 428 CB LEU 212
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     ATOM 429 CG LEU 212
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                                71.271 54.626 32.047 1.00 43.83
     ATOM 430 CD1 LEU 212
                                71.900 57.007 32.502 1.00 44.93
     ATOM 431 CD2 LEU 212
     ATOM 432 C LEU 212
                               72.448 55.050 28.133 1.00 37.61
                               71.318 54.805 27.719 1.00 33.71
     ATOM 433 O LEU 212
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                               73.360 55.670 27.393 1.00 41.23
            434 N GLU 213
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                                73.068 56.084 26.023 1.00 43.48
     ATOM 435 CA GLU 213
                                74.181 56.986 25.481 1.00 47.66
            436 CB GLU 213
     ATOM
                                73.919 57.494 24.065 1.00 56.87
            437 CG GLU 213
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                                75.121 58.180 23.433 1.00 60.87
            438 CD GLU 213
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                                76.258 57.996 23.924 1.00 60.37
            439 OE1 GLU 213
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                                74.921 58.894 22.423 1.00 61.13
            440 OE2 GLU 213
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                               72.889 54.880 25.102 1.00 39.29
            441 C GLU 213
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     ATOM
            442 O GLU 213
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            444 CA ALA 214
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                                74.946 51.817 24.711 1.00 30.70
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                               72.454 51.938 24.718 1.00 31.96
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                               72.151 51.798 26.003 1.00 28.47
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            449 CA PHE 215
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                                70.819 51.223 27.962 1.00 23.73
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             451 CG PHE 215
            452 CD1 PHE 215
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                                68.423 51.301 28.712 1.00 19.74
             453 CD2 PHE 215
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                                68.477 48.606 29.391 1.00 20.75
             454 CE1 PHE 215
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                                67.290 50.698 29.245 1.00 21.02
            455 CE2 PHE 215
     ATOM
                                67.318 49.346 29.586 1.00 19.50
            456 CZ PHE 215
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                               69.730 51.742 25.771 1.00 34.64
            457 C PHE 215
     ATOM
                               68.872 51.034 25.239 1.00 39.86
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     ATOM 458 O PHE 215
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            460 CA SER 216
    ATOM
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            461 CB SER 216
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                               67.537 55.987 25.193 1.00 48.33
            462 OG SER 216
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            463 C SER 216
            464 O SER 216
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            466 CA GLU 217
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    ATOM 468 CG GLU 217
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    ATOM 471 OE2 GLU 217
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            473 O GLU 217
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                               69.395 50.740 22.093 1.00 30.27
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            476 CB PHE 218
    ATOM 477 CG PHE 218
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            478 CD1 PHE 218
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                                71.495 48.301 21.087 1.00 24.78
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            479 CD2 PHE 218
            480 CE1 PHE 218
                                73.458 48.215 23.040 1.00 24.08
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     ATOM
                               73.818 48.187 21.697 1.00 25.04
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            482 CZ PHE 218
            483 C PHE 218
                               67.381 49.281 22.261 1.00 28.23
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                               66.639 48.605 21.543 1.00 33.52
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            485 N THR 219
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                                65.515 49.913 23.666 1.00 29.28
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            486 CA THR 219
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            487 CB THR 219
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            488 OG1 THR 219
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            489 CG2 THR 219
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                               64.660 50.612 22.615 1.00 33.29
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            490 C THR 219
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            491 O THR 219
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            493 CA LYS 220
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                               65.506 53.334 20.236 1.00 44.67
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            494 CB LYS 220
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            495 CG LYS 220
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            496 CD LYS 220
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            498 NZ LYS 220
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                                62.395 55.668 17.905 1.00 66.08
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            499 C LYS 220
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                               63.021 51.446 19.173 1.00 37.18
            500 O LYS 220
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            501 N ILE 221
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     ATOM
             502 CA ILE 221
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                               65.756 48.996 17.457 1.00 34.41
             503 CB ILE 221
     ATOM
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             504 CG2 ILE 221
     ATOM
             505 CG1 ILE 221
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                               67.984 47.752 17.338 1.00 31.12
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                              64.002 47.971 18.888 1.00 38.22
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                              63.499 47.181 18.089 1.00 38.90
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                               63.046 43.386 17.862 1.00 20.57
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           533 CB ALA 225
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                               60.455 41.323 17.544 1.00 25.07
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                              60.296 42.828 19.202 1.00 22.61
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     ATOM 537 CA ILE 226
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     ATOM 553 CB ARG 228
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     ATOM 556 NE ARG 228
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                               61.729 44.328 13.973 1.00 36.35
     ATOM 558 NH1 ARG 228
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            571 CB VAL 230
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            572 CG1 VAL 230
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            576 N ASP 231
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                               54.169 39.309 13.568 1.00 22.15
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                               53.620 40.684 13.921 1.00 29.49
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                                52.587 40.767 14.624 1.00 30.93
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            583 O ASP 231
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            586 CB PHE 232
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            587 CG PHE 232
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                               58,520 30.824 13.858 1.00 21.61
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            597 CB ALA 233
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                               52,609 33,040 15,917 1.00 22.04
            598 C ALA 233
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                               52.084 31.948 15.697 1.00 22.86
            599 O ALA 233
     ATOM
            600 N LYS 234
                               51.978 34.195 15.743 1.00 25.04
     ATOM
                                50.593 34.248 15.298 1.00 27.68
            601 CA LYS 234
     ATOM
     ATOM
            602 CB LYS 234
                                50.096 35.691 15.292 1.00 31.41
                                49.845 36.248 16.682 1.00 40.37
            603 CG LYS 234
     ATOM
45
                                49.212 37.626 16.604 1.00 57.53
            604 CD LYS 234
     ATOM
                                48.772 38.112 17.974 1.00 64.28
            605 CE LYS 234
     ATOM
                                48.164 39.473 17.904 1.00 67.19
            606 NZ LYS 234
     ATOM
                               50.358 33.588 13.939 1.00 26.42
             607 C LYS 234
     ATOM
                               49.269 33.067 13.674 1.00 31.34
            608 O LYS 234
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51.382 33.588 13.093 1.00 24.38
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                               52.244 33.664 10.805 1.00 24.92
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    ATOM
                               51.908 35.127 10.583 1.00 22.41
            612 CG LYS 235
    ATOM
     ATOM 613 CD LYS 235
                               52.843 35.775 9.588 1.00 29.38
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            614 CE LYS 235
                               52.481 37.234 9.395 1.00 33.49
     ATOM
                               53.354 37.869 8.376 1.00 40.13
     ATOM 615 NZ LYS 235
                              51.470 31.469 11.759 1.00 30.02
     ATOM 616 C LYS 235
                              51.417 30.838 10.699 1.00 30.37
           617 O LYS 235
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     ATOM 618 N LEU 236
                              51.722 30.889 12.930 1.00 32.39
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                               51.878 29.443 13.053 1.00 36.24
     ATOM 619 CA LEU 236
     ATOM 620 CB LEU 236
                               52.944 29.080 14.089 1.00 29.91
     ATOM 621 CG LEU 236
                               54.373 29.516 13.765 1.00 24.69
                                55.299 29.054 14.877 1.00 22.71
     ATOM 622 CD1 LEU 236
                                54.811 28.942 12.427 1.00 24.48
     ATOM 623 CD2 LEU 236
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                              50.520 28.891 13.470 1.00 41.22
     ATOM 624 C LEU 236
     ATOM 625 O LEU 236
                              49.936 29.333 14.467 1.00 41.45
                               50.012 27.895 12.729 1.00 47.86
     ATOM 626 N PRO 237
     ATOM 627 CD PRO 237
                               50.739 27.190 11.657 1.00 49.32
     ATOM 628 CA PRO 237
                               48.713 27.262 12.992 1.00 50.28
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                               48.669 26.128 11.962 1.00 55.25
     ATOM 629 CB PRO 237
     ATOM 630 CG PRO 237
                               50.135 25.818 11.706 1.00 54.08
     ATOM 631 C PRO 237
                              48.495 26.751 14.422 1.00 47.94
                               47.533 27.134 15.087 1.00 42.48
     ATOM 632 O PRO 237
     ATOM 633 N MET 238
                               49.415 25.927 14.906 1.00 49.51
25
                               49.306 25.354 16.245 1.00 53.49
     ATOM 634 CA MET 238
                                50.379 24.275 16.424 1.00 52.52
     ATOM 635 CB MET 238
     ATOM 636 CG MET 238
                                50.028 22.959 15.728 1.00 56.00
                                51.443 21.961 15.204 1.00 50.16
            637 SD MET 238
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                               50.896 21.440 13.552 1.00 55.71
     ATOM 638 CE MET 238
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            639 C MET 238
                               48.930 26.058 18.515 1.00 54.72
     ATOM
            640 O MET 238
            641 N PHE 239
                               49.803 27.578 17.101 1.00 50.11
     ATOM
                               49.917 28.619 18.117 1.00 41.11
            642 CA PHE 239
     ATOM
     ATOM 643 CB PHE 239
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                               51.336 30.607 18.826 1.00 30.25
     ATOM 644 CG PHE 239
                                52.127 30.332 19.937 1.00 25.66
            645 CD1 PHE 239
     ATOM
                                50.786 31.878 18.690 1.00 26.30
            646 CD2 PHE 239
     ATOM
     ATOM 647 CE1 PHE 239
                                52.368 31.307 20.896 1.00 30.28
                                51.019 32.862 19.644 1.00 30.49
     ATOM
            648 CE2 PHE 239
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                               51.813 32.576 20.750 1.00 29.00
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            649 CZ PHE 239
            650 C PHE 239
                               48.647 29.434 18.337 1.00 35.65
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                               48.151 29.521 19.457 1.00 30.27
            651 O PHE 239
     ATOM
     ATOM
            652 N SER 240
                               48.133 30.037 17.272 1.00 36.49
            653 CA SER 240
                               46.936 30.866 17.359 1.00 36.37
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     ATOM
                               46.622 31.466 15.994 1.00 35.87
            654 CB SER 240
     ATOM
            655 C SER 240
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     ATOM
                              44.784 30.789 18.438 1.00 37.47
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            656 O SER 240
                               45.713 28.814 17.889 1.00 43.00
            657 N GLU 241
     ATOM
                              44.605 28.004 18.404 1.00 46.31
            658 CA GLU 241
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44.714 26.566 17.881 1.00 55.84
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            660 CG GLU 241
     ATOM
                               45.141 25.015 15.900 1.00 74.99
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            661 CD GLU 241
                                45.835 24.299 16.658 1.00 77.81
            662 OE1 GLU 241
    ATOM
                                44.765 24.629 14.770 1.00 70.58
            663 OE2 GLU 241
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     ATOM
     ATOM
            664 C GLU 241
                               44.587 27.961 19.933 1.00 42.60
                               43.541 27.740 20.545 1.00 43.23
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                              45.762 28.125 20.535 1.00 39.31
     ATOM 666 N LEU 242
                               45.926 28.086 21.987 1.00 34.54
     ATOM
           667 CA LEU 242
     ATOM 668 CB LEU 242
                               47.417 28.109 22.344 1.00 28.35
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     ATOM 669 CG LEU 242
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                                49.750 27.307 22.180 1.00 20.72
     ATOM 670 CD1 LEU 242
                                47.902 25.661 22.500 1.00 24.97
     ATOM 671 CD2 LEU 242
                              45.242 29.240 22.711 1.00 32.23
     ATOM 672 C LEU 242
                              44.956 30.282 22.119 1.00 31.50
           673 O LEU 242
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     ATOM
     ATOM 674 N PRO 243
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                               45.118 27.843 24.827 1.00 31.68
     ATOM 675 CD PRO 243
           676 CA PRO 243
                               44.309 30.134 24.773 1.00 34.39
     ATOM
     ATOM 677 CB PRO 243
                               44.092 29.498 26.154 1.00 32.34
                               44.081 28.026 25.892 1.00 33.80
     ATOM 678 CG PRO 243
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                              45.300 31.303 24.873 1.00 35.56
     ATOM
            679 C PRO 243
                               46.517 31.082 24.897 1.00 34.99
     ATOM 680 O PRO 243
            681 N CYS 244
                               44.791 32.532 24.946 1.00 34.23
     ATOM
                               45.648 33.714 25.062 1.00 37.03
           682 CA CYS 244
     ATOM
                               44.820 34.960 25.376 1.00 43.49
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     ATOM 683 CB CYS 244
                               43.820 35.531 24.007 1.00 71.28
     ATOM 684 SG CYS 244
                               46.716 33.555 26.135 1.00 34.99
           685 C CYS 244
     ATOM
                               47.894 33.802 25.882 1.00 37.49
     ATOM 686 O CYS 244
     ATOM 687 N GLU 245
                               46.305 33.125 27.326 1.00 33.03
                                47.249 32.944 28.424 1.00 35.72
     ATOM 688 CA GLU 245
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                               46.559 32.469 29.716 1.00 37.85
     ATOM 689 CB GLU 245
                                45.294 31.633 29.549 1.00 46.81
     ATOM 690 CG GLU 245
                                44.029 32.478 29.480 1.00 44.81
     ATOM 691 CD GLU 245
     ATOM 692 OE1 GLU 245
                                43.606 33.012 30.527 1.00 33.05
     ATOM 693 OE2 GLU 245
                                43.454 32.599 28.377 1.00 48.22
35
                               48.414 32.035 28.047 1.00 32.29
     ATOM 694 C GLU 245
     ATOM 695 O GLU 245
                               49.558 32.319 28.399 1.00 35.92
                              48.134 30.975 27.295 1.00 30.64
     ATOM 696 N ASP 246
                               49.182 30.058 26.855 1.00 28.23
     ATOM 697 CA ASP 246
                               48.575 28.809 26.208 1.00 30.51
            698 CB ASP 246
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     ATOM
            699 CG ASP 246
                               48.213 27.737 27.222 1.00 33.18
     ATOM
            700 OD1 ASP 246
                                48.265 28.006 28.439 1.00 31.26
     ATOM
                                47.884 26.613 26.796 1.00 33.85
     ATOM
            701 OD2 ASP 246
                              50.104 30.757 25.860 1.00 30.10
     ATOM
            702 C ASP 246
     ATOM
            703 O ASP 246
                               51.330 30.651 25.950 1.00 27.08
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            704 N GLN 247
                               49.500 31.477 24.918 1.00 30.39
     ATOM
                                50.249 32.208 23.901 1.00 29.08
     ATOM
            705 CA GLN 247
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            706 CB GLN 247
     ATOM
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            707 CG GLN 247
     ATOM
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            708 CD GLN 247
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            709 OE1 GLN 247
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            710 NE2 GLN 247
    ATOM
           711 C GLN 247
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    ATOM
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           712 O GLN 247
    ATOM
                              50.661 33.921 25.552 1.00 27.81
    ATOM 713 N ILE 248
    ATOM
           714 CA ILE 248
                              51.431 34.908 26.295 1.00 29.41
                              50.525 35.662 27.303 1.00 28.96
    ATOM 715 CB ILE 248
    ATOM 716 CG2 ILE 248
                               51.356 36.476 28.279 1.00 28.67
    ATOM
           717 CG1 ILE 248
                               49.555 36.571 26.543 1.00 28.83
                               48.514 37.236 27.420 1.00 30.76
    ATOM 718 CD1 ILE 248
10
                              52.618 34.259 27.006 1.00 28.39
    ATOM 719 C ILE 248
                              53.759 34.715 26.869 1.00 27.88
    ATOM 720 O ILE 248
    ATOM 721 N ILE 249
                              52.356 33.177 27.732 1.00 26.07
    ATOM 722 CA ILE 249
                              53.413 32.474 28.454 1.00 27.37
                              52.839 31.294 29.281 1.00 30.32
    ATOM 723 CB ILE 249
15
                               53.958 30.425 29.840 1.00 31.29
    ATOM 724 CG2 ILE 249
                               51.987 31.831 30.429 1.00 30.31
    ATOM 725 CG1 ILE 249
                               51.295 30.753 31.230 1.00 31.30
    ATOM 726 CD1 ILE 249
    ATOM 727 C ILE 249
                              54.510 31.974 27.509 1.00 28.63
                              55.701 32.100 27.808 1.00 29.59
    ATOM 728 O ILE 249
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                              54.110 31.442 26.357 1.00 29.03
    ATOM 729 N LEU 250
                               55.068 30.934 25.380 1.00 22.44
    ATOM 730 CA LEU 250
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    ATOM 731 CB LEU 250
                               53.665 28.866 24.687 1.00 23.20
    ATOM 732 CG LEU 250
                                52.951 28.273 23.502 1.00 20.36
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    ATOM 733 CD1 LEU 250
    ATOM 734 CD2 LEU 250
                                54.685 27.880 25.238 1.00 19.45
                              55,919 32.055 24.794 1.00 18.97
    ATOM 735 C LEU 250
                              57.133 31.903 24.648 1.00 18.37
    ATOM 736 O LEU 250
                              55.291 33.180 24.468 1.00 20.63
    ATOM 737 N LEU 251
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    ATOM 738 CA LEU 251
    ATOM 739 CB LEU 251
                               55.065 35.412 23.449 1.00 22.92
    ATOM
           740 CG LEU 251
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    ATOM 741 CD1 LEU 251
                               53.342 36.167 21.821 1.00 32.13
            742 CD2 LEU 251
                                55.389 34.981 21.009 1.00 22.46
     ATOM
                              57.026 34.875 24.930 1.00 27.23
    ATOM 743 C LEU 251
35
                              58.202 35.078 24.614 1.00 26.48
    ATOM 744 O LEU 251
                              56.561 35.094 26.156 1.00 27.34
    ATOM 745 N LYS 252
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           746 CA LYS 252
    ATOM
    ATOM 747 CB LYS 252
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            748 CG LYS 252
                               55.570 36.783 28.530 1.00 35.06
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     ATOM
           749 CD LYS 252
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     ATOM
            750 CE LYS 252
                               54.124 38.191 30.003 1.00 53.05
     ATOM
                               53.677 38.451 31.398 1.00 64.03
            751 NZ LYS 252
     ATOM
            752 C LYS 252
                              58.605 34.647 27.405 1.00 27.66
     ATOM
            753 O LYS 252
                              59.734 35.076 27.646 1.00 33.16
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     ATOM
                               58.344 33.357 27.243 1.00 24.50
            754 N GLY 253
     ATOM
                              59.386 32.364 27.402 1.00 22.33
     ATOM
            755 CA GLY 253
            756 C GLY 253
                               60.423 32.273 26.297 1.00 23.99
     ATOM
                               61.589 32.016 26.581 1.00 30.77
            757 O GLY 253
     ATOM
     ATOM 758 N CYS 254
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60.986 32.405 23.934 1.00 20.75
            759 CA CYS 254
    ATOM
                                60.386 31.494 22.868 1.00 24.86
            760 CB CYS 254
     ATOM
                               58.996 32.276 22.014 1.00 25.55
            761 SG CYS 254
    ATOM
                               61.399 33.702 23.242 1.00 23.79
    ATOM
            762 C CYS 254
            763 O CYS 254
                               62.262 33.685 22.357 1.00 22.18
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    ATOM
            764 N CYS 255
                               60.788 34.814 23.625 1.00 19.49
    ATOM
                                61.084 36.085 22.981 1.00 21.08
            765 CA CYS 255
    ATOM
                                60.336 37.220 23.669 1.00 18.21
            766 CB CYS 255
    ATOM
            767 SG CYS 255
                               60.264 38.713 22.677 1.00 22.96
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            768 C CYS 255
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            769 O CYS 255
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            770 N MET 256
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            771 CA MET 256
                                64.741 36.706 23.895 1.00 20.50
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                                65.322 36.801 25.312 1.00 22.50
            772 CB MET 256
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                                66.808 37.139 25.354 1.00 16.67
            773 CG MET 256
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    ATOM
                                67.205 38.732 24.605 1.00 24.46
            774 SD MET 256
    ATOM
            775 CE MET 256
                                69.027 38.764 24.791 1.00 19.21
    ATOM
                               65.510 35.667 23.072 1.00 18.38
    ATOM
            776 C MET 256
            777 O MET 256
                               66.401 36.005 22.293 1.00 17.68
    ATOM
            778 N GLU 257
                               65.149 34.404 23.248 1.00 20.33
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    ATOM
            779 CA GLU 257
                                65.779 33.308 22.526 1.00 21.08
    ATOM
            780 CB GLU 257
                                65.148 31.982 22.943 1.00 22.28
     ATOM
                                65.374 31.640 24.411 1.00 34.68
            781 CG GLU 257
     ATOM
                                64.515 30.486 24.907 1.00 43.20
    ATOM
            782 CD GLU 257
            783 OE1 GLU 257
                                63.823 29.836 24.091 1.00 42.14
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           784 OE2 GLU 257
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                               65.650 33.503 21.018 1.00 19.26
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            786 O GLU 257
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                               64.199 34.065 19.141 1.00 18.09
            788 CA ILE 258
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            789 CB ILE 258
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     ATOM
            790 CG2 ILE 258
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     ATOM
            791 CG1 ILE 258
                               62.032 32.771 19.021 1.00 13.80
     ATOM
                                60.544 32.714 18.695 1.00 13.21
            792 CD1 ILE 258
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            793 C ILE 258
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     ATOM
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            794 O ILE 258
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     ATOM
            795 N MET 259
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     ATOM
            796 CA MET 259
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            797 CB MET 259
     ATOM
                                63.782 39.159 19.894 1.00 17.66
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     ATOM
            798 CG MET 259
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     ATOM
            799 SD MET 259
            800 CE MET 259
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     ATOM
                               67.111 37.397 18.973 1.00 19.51
            801 C MET 259
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     ATOM
            802 O MET 259
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            803 N SER 260
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                                69.056 36.324 19.947 1.00 16.90
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     ATOM
            805 CB SER 260
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                                69.093 36.455 22.352 1.00 22.98
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            806 OG SER 260
                               69.471 35.487 18.746 1.00 14.52
            807 C SER 260
     ATOM
                               70.496 35.761 18.129 1.00 22.82
     ATOM
            808 O SER 260
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68.663 34.490 18.397 1.00 16.50
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            811 CB LEU 261
    ATOM
                               67.890 31.708 15.812 1.00 14.47
    ATOM 812 CG LEU 261
                               69.159 30.877 15.728 1.00 16.76
    ATOM 813 CD1 LEU 261
                               66.672 30.806 15.793 1.00 14.06
    ATOM 814 CD2 LEU 261
                              68.959 34.519 15.992 1.00 20.40
    ATOM 815 C LEU 261
                              69.885 34.450 15.181 1.00 22.00
    ATOM 816 O LEU 261
    ATOM 817 N ARG 262
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    ATOM 818 CA ARG 262
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                               66.530 37.067 14.782 1.00 20.29
    ATOM 819 CB ARG 262
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    ATOM 820 CG ARG 262
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    ATOM 821 CD ARG 262
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    ATOM 822 NE ARG 262
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    ATOM 823 CZ ARG 262
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    ATOM 824 NH1 ARG 262
    ATOM 825 NH2 ARG 262
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                              69.035 37.154 14.561 1.00 22.66
    ATOM 826 C ARG 262
    ATOM 827 O ARG 262
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            828 N ALA 263
                              69.625 37.545 15.689 1.00 23.52
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    ATOM
                              70.820 38.386 15.677 1.00 22.37
    ATOM 829 CA ALA 263
                               70.986 39.089 17.018 1.00 22.76
    ATOM 830 CB ALA 263
    ATOM 831 C ALA 263
                              72.052 37.530 15.366 1.00 22.85
                              72.882 37.897 14.529 1.00 25.50
            832 O ALA 263
    ATOM
                               72.131 36.365 16.005 1.00 21.68
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            834 CA ALA 264
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                               73.092 34.256 16.763 1.00 15.97
    ATOM 835 CB ALA 264
                              73.401 34.957 14.382 1.00 23.11
    ATOM 836 C ALA 264
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     ATOM 837 O ALA 264
                              72.293 34.679 13.697 1.00 22.94
    ATOM 838 N VAL 265
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     ATOM 839 CA VAL 265
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    ATOM
            840 CB VAL 265
                                70.751 32.330 12.638 1.00 26.27
    ATOM
            841 CG1 VAL 265
            842 CG2 VAL 265
                                69.907 34.527 11.797 1.00 26.64
     ATOM
            843 C VAL 265
                              72.761 35.373 11.369 1.00 28.81
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    ATOM
    ATOM 844 O VAL 265
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                               72.830 36.587 11.915 1.00 31.83
     ATOM 845 N ARG 266
                               73.210 37.774 11.150 1.00 33.19
            846 CA ARG 266
    ATOM
                               72.141 38.861 11.258 1.00 31.67
     ATOM 847 CB ARG 266
            848 CG ARG 266
                               70.986 38.623 10.320 1.00 26.82
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     ATOM
            849 CD ARG 266
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     ATOM
     ATOM
            850 NE ARG 266
                               68.955 39.532 9.361 1.00 38.15
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     ATOM
            851 CZ ARG 266
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     ATOM
            853 NH2 ARG 266
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     ATOM
            854 C ARG 266
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     ATOM
            855 O ARG 266
            856 N TYR 267
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                              77.283 36.640 13.440 1.00 32.37
            858 CB TYR 267
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            863 CE2 TYR 267
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            865 OH TYR 267
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                               77.609 36,943 10.410 1.00 36.48
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            867 O TYR 267
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                                80.773 41.847 8.280 1.00 50.24
            873 OD2 ASP 268
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    ATOM
                              80.737 38.846 10.466 1.00 42.51
    ATOM
            874 C ASP 268
            875 O ASP 268
                              81.305 39.645 11.208 1.00 42.75
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            876 N PRO 269
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    ATOM
                               80.770 36.697 9.146 1.00 42.66
    ATOM
            877 CD PRO 269
            878 CA PRO 269
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    ATOM
                               81.631 35.506 9.458 1.00 43.33
            880 CG PRO 269
    ATOM
                               83.710 38.492 10.004 1.00 50.31
            881 C PRO 269
    ATOM
                               84.630 38.800 10.761 1.00 49.83
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            883 N ALA 270
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            891 OG SER 271
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            892 C SER 271
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                               83.051 41.162 12.619 1.00 48.96
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            895 CA ASP 272
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            896 CB ASP 272
    ATOM
                               84.142 40.064 16.131 1.00 47.66
    ATOM
            897 CG ASP 272
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            898 OD1 ASP 272
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            899 OD2 ASP 272
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                               80.652 41.551 13.915 1.00 39.79
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     ATOM
            903 CA THR 273
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            904 CB THR 273
     ATOM
                                79.288 43.439 12.254 1.00 39.36
            905 OG1 THR 273
     ATOM
     ATOM
            906 CG2 THR 273
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            907 C THR 273
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                               78.151 40.546 13.408 1.00 33.79
     ATOM
            908 O THR 273
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            911 CB LEU 274
    ATOM
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            912 CG LEU 274
            913 CD1 LEU 274
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            914 CD2 LEU 274
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           915 C LEU 274
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                               75.171 43.478 14.601 1.00 37.47
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           916 O LEU 274
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    ATOM
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            918 CA THR 275
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                               72.824 42.674 11.542 1.00 35.14
           919 CB THR 275
    ATOM
                                74.108 42.590 10.909 1.00 39.50
    ATOM 920 OG1 THR 275
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    ATOM 921 CG2 THR 275
                               71.699 42.746 13.793 1.00 30.92
    ATOM 922 C THR 275
                               71.100 41.670 13.845 1.00 36.53
    ATOM 923 O THR 275
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                               71.291 43.835 14.434 1.00 28.10
    ATOM 924 N LEU 276
                               70.051 43.868 15.192 1.00 27.78
    ATOM 925 CA LEU 276
                               70.205 44.780 16.420 1.00 22.51
    ATOM 926 CB LEU 276
    ATOM 927 CG LEU 276
                               71.383 44.532 17.373 1.00 25.89
                                71.225 45.408 18.608 1.00 20.70
    ATOM 928 CD1 LEU 276
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                                71.456 43.069 17.782 1.00 20.79
    ATOM 929 CD2 LEU 276
                              68.930 44.376 14.296 1.00 27.27
    ATOM 930 C LEU 276
                               69.068 45.430 13.672 1.00 29.06
           931 O LEU 276
    ATOM
     ATOM 932 N SER 277
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    ATOM 933 CA SER 277
                               66.697 43.957 13.366 1.00 28.63
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                               65.990 45.177 13.967 1.00 27.78
            934 CB SER 277
    ATOM
                               65.561 44.905 15.290 1.00 22.65
     ATOM
            935 OG SER 277
            936 C SER 277
                              67.067 44.209 11.897 1.00 30.31
     ATOM
                               66.374 44.939 11.181 1.00 28.52
            937 O SER 277
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                               68.168 43.597 11.465 1.00 31.24
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            938 N GLY 278
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            939 CA GLY 278
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                               68.999 45.178 9.706 1.00 44.55
            940 C GLY 278
     ATOM
            941 O GLY 278
                               69.104 45.479 8.517 1.00 46.66
     ATOM
                               69.234 46.046 10.686 1.00 43.47
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            942 N GLU 279
            943 CA GLU 279
                                69.566 47.435 10.387 1.00 43.87
     ATOM
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            944 CB GLU 279
                                68.314 48.312 10.515 1.00 44.28
     ATOM
            945 CG GLU 279
                                67.703 48.322 11.908 1.00 52.30
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     ATOM
            946 CD GLU 279
                                66.440 49.159 12.001 1.00 60.23
            947 OE1 GLU 279
                                66.398 50.074 12.853 1.00 63.06
     ATOM
            948 OE2 GLU 279
                                65.485 48.894 11.238 1.00 65.67
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            949 C GLU 279
                               70.700 48.038 11.216 1.00 42.40
     ATOM
                               71.330 49.001 10.787 1.00 43.89
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     ATOM
                               70.977 47.472 12.388 1.00 40.86
     ATOM
            951 N MET 280
            952 CA MET 280
                                72.027 48.009 13.248 1.00 32.80
     ATOM
                                71.435 48.415 14.603 1.00 29.25
            953 CB MET 280
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                                72.384 49.193 15.506 1.00 31.64
     ATOM
            954 CG MET 280
            955 SD MET 280
                                71.830 49.235 17.232 1.00 34.02
     ATOM
            956 CE MET 280
                                70.566 50.495 17.197 1.00 26.56
     ATOM
                               73.172 47.033 13.465 1.00 32.77
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             957 C MET 280
            958 O MET 280
                               72.983 45,971 14.058 1.00 34.61
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                               76.519 46.727 12.023 1.00 34.42
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                               76.125 46.950 14.482 1.00 36.76
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                               76.416 48.129 14.693 1.00 34.59
    ATOM
            963 O ALA 281
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                               76.275 45.993 15.390 1.00 37.16
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                               76.798 46.263 16.721 1.00 37.83
            965 CA VAL 282
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                               75.692 46.023 17.780 1.00 37.58
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            966 CB VAL 282
            967 CG1 VAL 282
                                76.219 46.271 19.175 1.00 48.99
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            968 CG2 VAL 282
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                               78.081 44.230 16.660 1.00 39.16
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            970 O VAL 282
                              78.989 45.993 17.735 1.00 38.75
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    ATOM
                               80.205 45.287 18.136 1.00 42.18
            972 CA LYS 283
    ATOM
                               81.428 46.208 18.045 1.00 47.46
            973 CB LYS 283
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    ATOM
                               81.803 46.617 16.632 1.00 51.71
            974 CG LYS 283
     ATOM
                               83.092 47.416 16.618 1.00 59.26
            975 CD LYS 283
     ATOM
            976 CE LYS 283
                               83,481 47.813 15.202 1.00 62.52
     ATOM
                               82,492 48,742 14,588 1.00 66,27
            977 NZ LYS 283
    ATOM
            978 C LYS 283
                              80.075 44.746 19.559 1.00 38.78
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                               79.283 45.257 20.356 1.00 40.63
    ATOM
            979 O LYS 283
                               80.900 43.753 19.881 1.00 36.01
            980 N ARG 284
     ATOM
                                80.908 43.104 21.189 1.00 38.62
            981 CA ARG 284
     ATOM
                                82.150 42.224 21.327 1.00 38.83
     ATOM
            982 CB ARG 284
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     ATOM
            983 CG ARG 284
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            984 CD ARG 284
     ATOM
                                83.506 39.120 19.644 1.00 45.18
     ATOM
            985 NE ARG 284
                                83.259 37.905 20.128 1.00 44.79
     ATOM
            986 CZ ARG 284
                                83.005 37.739 21.421 1.00 41.84
            987 NH1 ARG 284
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                                 83.271 36.852 19.319 1.00 42.27
            988 NH2 ARG 284
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                               80.829 44.051 22.385 1.00 41.18
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                               79.995 43.867 23.274 1.00 44.38
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     ATOM
                               81.703 45.052 22.416 1.00 38.71
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                                81.724 46.002 23.525 1.00 37.18
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            992 CA GLU 285
            993 CB GLU 285
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                               79.920 47.245 22.463 1.00 32.01
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            996 N GLN 286
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            997 CA GLN 286
     ATOM
            998 CB GLN 286
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     ATOM 999 CG GLN 286
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                                79.277 49.761 18.964 1.00 44.79
     ATOM 1000 CD GLN 286
                                 79.103 48.910 18.089 1.00 42.21
     ATOM 1001 OE1 GLN 286
     ATOM 1002 NE2 GLN 286
                                 79.215 51.063 18.719 1.00 47.53
                                77.484 47.355 23.002 1.00 33.08
     ATOM 1003 C GLN 286
45
                                76.770 47.929 23.827 1.00 30.95
     ATOM 1004 O GLN 286
     ATOM 1005 N LEU 287
                               77.245 46.114 22.579 1.00 31.49
                                76.095 45.350 23.068 1.00 31.01
     ATOM 1006 CA LEU 287
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     ATOM 1008 CG LEU 287
                                74.498 43.780 21.661 1.00 27.34
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     ATOM 1010 CD2 LEU 287
                               76.298 44.986 24.538 1.00 32.80
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    ATOM 1012 O LEU 287
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                               77.536 44.641 24.885 1.00 32.54
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    ATOM 1013 N LYS 288
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     ATOM 1014 CA LYS 288
                               79.376 43.893 26.315 1.00 31.24
     ATOM 1015 CB LYS 288
                               79.834 43.382 27.662 1.00 34.69
     ATOM 1016 CG LYS 288
     ATOM 1017 CD LYS 288
                               81.227 42.784 27.574 1.00 37.69
     ATOM 1018 CE LYS 288
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                               82.883 41.369 28.786 1.00 49.63
     ATOM 1019 NZ LYS 288
     ATOM 1020 C LYS 288
                               77.611 45.448 27.189 1.00 28.74
                               76.827 45.319 28.129 1.00 34.45
     ATOM 1021 O LYS 288
                               78.190 46.602 26.882 1.00 26.57
     ATOM 1022 N ASN 289
     ATOM 1023 CA ASN 289
                               78.011 47.803 27.691 1.00 30.84
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     ATOM 1024 CB ASN 289
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     ATOM 1025 CG ASN 289
                                80.437 48.485 27.570 1.00 35.16
                                80.700 47.718 28.499 1.00 42.54
     ATOM 1026 OD1 ASN 289
     ATOM 1027 ND2 ASN 289
                                81.371 48.998 26.784 1.00 32.82
                               76.602 48.371 27.620 1.00 35.05
     ATOM 1028 C ASN 289
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                               76.154 49.039 28.550 1.00 36.94
     ATOM 1029 O ASN 289
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                               75.909 48.113 26.515 1.00 32.43
                                74.556 48.614 26.345 1.00 28.66
     ATOM 1031 CA GLY 290
                               73.525 48.024 27.289 1.00 28.48
     ATOM 1032 C GLY 290
     ATOM 1033 O GLY 290
                               72.377 48.467 27.308 1.00 28.17
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                               72.969 46.408 28.980 1.00 29.19
     ATOM 1035 CA GLY 291
                               72.976 44.894 29.075 1.00 29.76
     ATOM 1036 C GLY 291
     ATOM 1037 O GLY 291
                               72.595 44.340 30.105 1.00 34.44
                               73.399 44.213 28.017 1.00 29.69
     ATOM 1038 N LEU 292
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     ATOM 1039 CA LEU 292
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     ATOM 1040 CB LEU 292
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     ATOM 1041 CG LEU 292
                                72.113 42.348 25.833 1.00 23.27
     ATOM 1042 CD1 LEU 292
                                72.202 41.580 24.532 1.00 22.24
     ATOM 1043 CD2 LEU 292
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                               74.530 42.125 28.861 1.00 29.22
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     ATOM 1045 O LEU 292
     ATOM 1046 N GLY 293
                               75.671 42.800 28.945 1.00 30.26
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     ATOM 1047 CA GLY 293
                               77.307 40.995 29.040 1.00 29.85
     ATOM 1048 C GLY 293
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                               77.460 40.951 27.820 1.00 32.37
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     ATOM 1050 N VAL 294
                               77.537 39.953 29.832 1.00 30.08
                                78.041 38.687 29.308 1.00 31.62
     ATOM 1051 CA VAL 294
     ATOM 1052 CB VAL 294
                                78.466 37.716 30.442 1.00 29.11
     ATOM 1053 CG1 VAL 294
                                79.649 38.292 31.191 1.00 31.37
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                                77.304 37.443 31.396 1.00 26.69
     ATOM 1054 CG2 VAL 294
     ATOM 1055 C VAL 294
                               77.079 37.978 28.351 1.00 32.81
     ATOM 1056 O VAL 294
                               77.496 37.095 27.591 1.00 33.00
     ATOM 1057 N VAL 295
                               75.801 38.356 28.380 1.00 30.45
                              74.814 37.752 27.487 1.00 28.02
     ATOM 1058 CA VAL 295
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ATOM 1059 CB VAL 295
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    ATOM 1060 CG1 VAL 295
                                73.016 37.903 29.232 1.00 20.10
    ATOM 1061 CG2 VAL 295
                               75.203 38.115 26.057 1.00 29.90
    ATOM 1062 C VAL 295
                               75.047 37.312 25.140 1.00 34.47
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    ATOM 1063 O VAL 295
    ATOM 1064 N SER 296
                               75.762 39.309 25.886 1.00 29.11
                               76.215 39.771 24.581 1.00 30.96
    ATOM 1065 CA SER 296
                               76.785 41.184 24.702 1.00 27.26
    ATOM 1066 CB SER 296
    ATOM 1067 OG SER 296
                               77.300 41.648 23.469 1.00 22.93
                               77.294 38.811 24.080 1.00 36.41
    ATOM 1068 C SER 296
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                               77.238 38.341 22.939 1.00 38.84
    ATOM 1069 O SER 296
                               78.254 38.501 24.954 1.00 35.29
    ATOM 1070 N ASP 297
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    ATOM 1071 CA ASP 297
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    ATOM 1072 CB ASP 297
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    ATOM 1073 CG ASP 297
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    ATOM 1074 OD1 ASP 297
                                80.999 38.861 27.532 1.00 45.15
    ATOM 1075 OD2 ASP 297
     ATOM 1076 C ASP 297
                               78.768 36.249 24.191 1.00 29.61
                               79.242 35.644 23.231 1.00 32.90
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                               77.738 35.804 24.903 1.00 27.85
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    ATOM 1078 N ALA 298
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    ATOM 1079 CA ALA 298
     ATOM 1080 CB ALA 298
                                75.998 34.258 25.657 1.00 21.67
                               76.462 34.539 23.202 1.00 28.26
     ATOM 1081 C ALA 298
     ATOM 1082 O ALA 298
                               76.648 33.579 22.446 1.00 30.19
    ATOM 1083 N ILE 299
                              75,744 35.606 22.853 1.00 25.20
25
                               75.119 35.708 21.537 1.00 23.46
     ATOM 1084 CA ILE 299
     ATOM 1085 CB ILE 299
                               74.200 36.944 21.427 1.00 21.63
                               73.491 36.946 20.078 1.00 22.20
     ATOM 1086 CG2 ILE 299
                                73.145 36.914 22.536 1.00 19.79
     ATOM 1087 CG1 ILE 299
                                72.245 38.139 22.578 1.00 18.33
     ATOM 1088 CD1 ILE 299
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     ATOM 1089 C ILE 299
                              76.181 35.752 20.444 1.00 26.28
                              76.043 35.095 19.414 1.00 31.72
     ATOM 1090 O ILE 299
                               77.247 36.512 20.675 1.00 29.35
     ATOM 1091 N PHE 300
                                78.338 36.613 19.709 1.00 29.01
     ATOM 1092 CA PHE 300
                                79.386 37.622 20.182 1.00 29.53
     ATOM 1093 CB PHE 300
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                                79.239 38.978 19.562 1.00 27.60
     ATOM 1094 CG PHE 300
     ATOM 1095 CD1 PHE 300
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     ATOM 1096 CD2 PHE 300
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     ATOM 1097 CE1 PHE 300
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     ATOM 1098 CE2 PHE 300
                                79.715 40.518 17.761 1.00 25.97
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     ATOM 1099 CZ PHE 300
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                               79.309 34.873 18.367 1.00 29.35
     ATOM 1101 O PHE 300
     ATOM 1102 N GLU 301
                               79.181 34.507 20.582 1.00 31.04
                                79.775 33.178 20.499 1.00 33.60
     ATOM 1103 CA GLU 301
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                                80.012 32.607 21.898 1.00 31.64
     ATOM 1104 CB GLU 301
                               78.851 32.265 19.696 1.00 33.90
     ATOM 1105 C GLU 301
                               79.315 31.473 18.872 1.00 33.33
     ATOM 1106 O GLU 301
                               77.546 32.386 19.935 1.00 31.13
     ATOM 1107 N LEU 302
     ATOM 1108 CA LEU 302
                              76.556 31.581 19.227 1.00 27.57
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75.150 31.842 19.776 1.00 25.24
    ATOM 1109 CB LEU 302
                                73.994 31.131 19.059 1.00 28.59
    ATOM 1110 CG LEU 302
                                74.066 29.634 19.299 1.00 25.52
    ATOM 1111 CD1 LEU 302
                                72,660 31,682 19,532 1.00 19.30
    ATOM 1112 CD2 LEU 302
                               76.601 31.904 17.739 1.00 26.80
    ATOM 1113 C LEU 302
                               76.682 31.003 16.904 1.00 27.81
    ATOM 1114 O LEU 302
                               76.576 33.195 17.416 1.00 26.47
    ATOM 1115 N GLY 303
                                76.611 33.624 16.030 1.00 26.99
    ATOM 1116 CA GLY 303
    ATOM 1117 C GLY 303
                               77.845 33.133 15.295 1.00 33.46
                               77.757 32.646 14.164 1.00 32.33
    ATOM 1118 O GLY 303
10
                               78.994 33.232 15.956 1.00 34.63
    ATOM 1119 N LYS 304
                                80.269 32.813 15.383 1.00 36.20
     ATOM 1120 CA LYS 304
                               81.399 33.115 16.372 1.00 41.96
     ATOM 1121 CB LYS 304
                                82.779 33.179 15.757 1.00 47.05
     ATOM 1122 CG LYS 304
                                83.800 33.610 16.796 1.00 59.47
    ATOM 1123 CD LYS 304
15
                               85.179 33.791 16.181 1.00 65.89
     ATOM 1124 CE LYS 304
     ATOM 1125 NZ LYS 304
                               85.182 34.863 15.144 1.00 71.01
                               80.276 31.332 14.992 1.00 33.17
     ATOM 1126 C LYS 304
     ATOM 1127 O LYS 304
                               80.752 30.974 13.913 1.00 34.44
                               79.739 30.482 15.861 1.00 31.40
     ATOM 1128 N SER 305
20
                               79.687 29.048 15.594 1.00 33.10
     ATOM 1129 CA SER 305
                               79.513 28.266 16.900 1.00 34.10
     ATOM 1130 CB SER 305
     ATOM 1131 OG SER 305
                                78.391 28.727 17.633 1.00 40.61
                               78.597 28.664 14.589 1.00 33.02
     ATOM 1132 C SER 305
                               78.771 27.718 13.816 1.00 35.32
25
     ATOM 1133 O SER 305
                               77.488 29.404 14.580 1.00 32.14
     ATOM 1134 N LEU 306
                                76.391 29.121 13.653 1.00 31.02
     ATOM 1135 CA LEU 306
                                75.138 29.936 13.996 1.00 22.76
     ATOM 1136 CB LEU 306
                                74.361 29.487 15.235 1.00 24.42
     ATOM 1137 CG LEU 306
                                73.094 30.311 15.380 1.00 23.13
     ATOM 1138 CD1 LEU 306
30
                                74.016 28.009 15.126 1.00 25.53
     ATOM 1139 CD2 LEU 306
     ATOM 1140 C LEU 306
                               76.780 29.354 12.198 1.00 33.11
                               76.161 28.796 11.293 1.00 32.60
     ATOM 1141 O LEU 306
                               77.821 30.153 11.975 1.00 36.12
     ATOM 1142 N SER 307
     ATOM 1143 CA SER 307
                                78.296 30,448 10.624 1.00 38.80
35
                                79.514 31.373 10.677 1.00 41.64
     ATOM 1144 CB SER 307
                                79.224 32.556 11.401 1.00 54.66
     ATOM 1145 OG SER 307
                               78.650 29.182 9.845 1.00 36.98
     ATOM 1146 C SER 307
                               78.302 29.055 8.669 1.00 42.87
     ATOM 1147 O SER 307
                               79.315 28.239 10.509 1.00 35.72
40
     ATOM 1148 N ALA 308
                                79.719 26.983 9.879 1.00 32.70
     ATOM 1149 CA ALA 308
                                80.683 26.227 10.782 1.00 33.88
     ATOM 1150 CB ALA 308
                               78.531 26.093 9.521 1.00 34.83
     ATOM 1151 C ALA 308
                               78.620 25.278 8.600 1.00 39.61
     ATOM 1152 O ALA 308
     ATOM 1153 N PHE 309
                               77.424 26.250 10.244 1.00 31.54
45
                                76.226 25.453 9.999 1.00 32.43
     ATOM 1154 CA PHE 309
                                75.259 25.558 11.182 1.00 30.89
     ATOM 1155 CB PHE 309
     ATOM 1156 CG PHE 309
                                75.718 24.826 12.415 1.00 33.73
                                76.769 25.314 13.183 1.00 40.48
     ATOM 1157 CD1 PHE 309
                                 75.091 23.654 12.816 1.00 35.96
50
     ATOM 1158 CD2 PHE 309
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ATOM 1159 CE1 PHE 309
                               77.189 24.643 14.334 1.00 37.87
                               75.502 22.975 13.962 1.00 38.44
     ATOM 1160 CE2 PHE 309
     ATOM 1161 CZ PHE 309
                               76.553 23.471 14.722 1.00 37.34
                              75.507 25.809 8.693 1.00 34.76
    ATOM 1162 C PHE 309
                              74.810 24.969 8.118 1.00 36.18
     ATOM 1163 O PHE 309
 5
     ATOM 1164 N ASN 310
                               75.693 27.040 8.218 1.00 35.80
                              75.060 27.506 6.980 1.00 41.00
     ATOM 1165 CA ASN 310
     ATOM 1166 CB ASN 310
                               75.705 26.852 5.755 1.00 51.94
     ATOM 1167 CG ASN 310
                               77.053 27.452 5.419 1.00 67.92
    ATOM 1168 OD1 ASN 310
                                77.139 28.439 4.687 1.00 77.32
10
     ATOM 1169 ND2 ASN 310
                                78.116 26.869 5.962 1.00 72.62
                               73.560 27.245 6.985 1.00 38.15
     ATOM 1170 C ASN 310
                               73.034 26.515 6.141 1.00 35.87
     ATOM 1171 O ASN 310
     ATOM 1172 N LEU 311
                               72.885 27.819 7.971 1.00 33.94
     ATOM 1173 CA LEU 311
                              71.450 27.651 8.111 1.00 32.09
15
     ATOM 1174 CB LEU 311
                               71.011 28.009 9.533 1.00 28.06
     ATOM 1175 CG LEU 311
                               71.656 27.301 10.724 1.00 26.38
                               71.092 27.883 12.012 1.00 23.56
     ATOM 1176 CD1 LEU 311
     ATOM 1177 CD2 LEU 311
                                71.409 25.801 10.651 1.00 21.24
                              70.705 28.542 7.124 1.00 33.00
     ATOM 1178 C LEU 311
20
                               71.173 29.630 6.782 1.00 35.47
     ATOM 1179 O LEU 311
                              69.569 28.057 6.638 1.00 27.78
     ATOM 1180 N ASP 312
                               68.749 28.841 5.733 1.00 27.06
     ATOM 1181 CA ASP 312
                               68.385 28.049 4.456 1.00 25.84
     ATOM 1182 CB ASP 312
                               67.580 26.778 4.724 1.00 25.67
25
     ATOM 1183 CG ASP 312
     ATOM 1184 OD1 ASP 312
                                67.124 26.541 5.860 1.00 28.20
     ATOM 1185 OD2 ASP 312
                                67.387 26.008 3.762 1.00 27.62
                              67.517 29.314 6.514 1.00 28.51
     ATOM 1186 C ASP 312
     ATOM 1187 O ASP 312
                              67.371 28.990 7.703 1.00 25.35
                              66.633 30.060 5.855 1.00 22.16
    ATOM 1188 N ASP 313
30
     ATOM 1189 CA ASP 313
                               65.430 30.589 6.494 1.00 21.37
                               64.625 31.431 5.499 1.00 25.11
     ATOM 1190 CB ASP 313
     ATOM 1191 CG ASP 313
                               65,380 32,666 5,025 1,00 31,54
     ATOM 1192 OD1 ASP 313
                                65.119 33.115 3.890 1.00 35.35
                                66.225 33.193 5.783 1.00 35.37
35
     ATOM 1193 OD2 ASP 313
                              64.524 29.535 7.120 1.00 21.11
     ATOM 1194 C ASP 313
                              63.904 29.783 8.158 1.00 23.68
     ATOM 1195 O ASP 313
                               64.440 28.367 6.489 1.00 22.88
     ATOM 1196 N THR 314
     ATOM 1197 CA THR 314
                              63.591 27.281 6.981 1.00 22.81
     ATOM 1198 CB THR 314
                               63.472 26.155 5.927 1.00 26.00
40
                               62.873 26.679 4.732 1.00 20.14
     ATOM 1199 OG1 THR 314
     ATOM 1200 CG2 THR 314
                                62.629 25.010 6.457 1.00 17.51
     ATOM 1201 C THR 314
                               64.086 26.706 8.310 1.00 19.46
                               63.312 26.529 9.247 1.00 19.33
     ATOM 1202 O THR 314
     ATOM 1203 N GLU 315
                               65.381 26.431 8.392 1.00 17.49
45
                                65.965 25.885 9.611 1.00 20.62
     ATOM 1204 CA GLU 315
                                67.426 25.514 9.358 1.00 14.39
     ATOM 1205 CB GLU 315
     ATOM 1206 CG GLU 315
                                67.539 24.339 8.400 1.00 13.07
     ATOM 1207 CD GLU 315
                                68.923 24.125 7.835 1.00 14.98
                              69.634 25.116 7.552 1.00 17.71
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     ATOM 1208 OE1 GLU 315
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ATOM 1209 OE2 GLU 315
                                69.287 22.948 7.651 1.00 17.88
                               65.810 26.883 10.762 1.00 20.57
     ATOM 1210 C GLU 315
                               65.368 26.518 11.854 1.00 18.43
    ATOM 1211 O GLU 315
                               66.096 28.154 10.488 1.00 19.19
    ATOM 1212 N VAL 316
                                65.955 29.203 11.490 1.00 16.53
    ATOM 1213 CA VAL 316
                                66.418 30.567 10.933 1.00 17.42
    ATOM 1214 CB VAL 316
                                66.149 31.687 11.940 1.00 13.89
    ATOM 1215 CG1 VAL 316
    ATOM 1216 CG2 VAL 316
                                67.900 30.506 10.594 1.00 14.31
                               64.488 29.291 11.927 1.00 19.53
    ATOM 1217 C VAL 316
                               64.191 29.448 13.110 1.00 19.86
    ATOM 1218 O VAL 316
10
    ATOM 1219 N ALA 317
                               63.575 29.159 10.970 1.00 19.02
                               62.145 29.215 11.254 1.00 16.95
    ATOM 1220 CA ALA 317
    ATOM 1221 CB ALA 317
                                61.357 29.239 9.951 1.00 17.68
    ATOM 1222 C ALA 317
                               61.674 28.047 12.126 1.00 14.13
                               60.875 28.228 13.045 1.00 15.34
    ATOM 1223 O ALA 317
15
     ATOM 1224 N LEU 318
                               62.154 26.847 11.819 1.00 17.41
                                61.769 25.653 12.569 1.00 19.10
    ATOM 1225 CA LEU 318
     ATOM 1226 CB LEU 318
                               62.186 24.398 11.802 1.00 18.21
                                61.443 24.209 10.473 1.00 19.02
     ATOM 1227 CG LEU 318
                                62.105 23.128 9.646 1.00 16.10
20
     ATOM 1228 CD1 LEU 318
                                59.987 23.875 10.735 1.00 11.32
     ATOM 1229 CD2 LEU 318
                               62.399 25.685 13.954 1.00 22.38
     ATOM 1230 C LEU 318
                               61.782 25.278 14.945 1.00 21.64
     ATOM 1231 O LEU 318
     ATOM 1232 N LEU 319
                               63.619 26.207 14.016 1.00 20.97
                                64.338 26.344 15.270 1.00 19.71
     ATOM 1233 CA LEU 319
25
                                65.715 26.951 15.005 1.00 20.56
     ATOM 1234 CB LEU 319
     ATOM 1235 CG LEU 319
                                66.722 27.036 16.152 1.00 32.05
     ATOM 1236 CD1 LEU 319
                                66.704 25.760 16.963 1.00 33.15
                                68.109 27.303 15.590 1.00 28.25
     ATOM 1237 CD2 LEU 319
                               63.496 27.254 16.164 1.00 20.66
30
     ATOM 1238 C LEU 319
                               63.215 26.920 17.313 1.00 24.47
     ATOM 1239 O LEU 319
                               63.026 28.365 15.604 1.00 19.25
     ATOM 1240 N GLN 320
                                62.191 29.307 16.346 1.00 19.02
     ATOM 1241 CA GLN 320
                                61.842 30.526 15.488 1.00 19.11
     ATOM 1242 CB GLN 320
                                63.032 31.377 15.101 1.00 20.02
     ATOM 1243 CG GLN 320
35
     ATOM 1244 CD GLN 320
                                62.665 32.562 14.224 1.00 23.65
                                63.487 33.445 13.997 1.00 22.68
     ATOM 1245 OE1 GLN 320
                                61.440 32.574 13.704 1.00 20.77
     ATOM 1246 NE2 GLN 320
                               60.905 28.635 16.811 1.00 20.52
     ATOM 1247 C GLN 320
     ATOM 1248 O GLN 320
                               60.465 28.845 17.938 1.00 22.04
40
                               60.306 27.825 15.942 1.00 21.01
     ATOM 1249 N ALA 321
                                59.069 27.128 16.280 1.00 16.83
     ATOM 1250 CA ALA 321
                                58.556 26.358 15.079 1.00 16.58
     ATOM 1251 CB ALA 321
     ATOM 1252 C ALA 321
                               59.288 26.185 17.462 1.00 18.15
                               58.427 26.069 18.344 1.00 13.03
     ATOM 1253 O ALA 321
45
                               60.442 25.523 17.481 1.00 14.89
     ATOM 1254 N VAL 322
     ATOM 1255 CA VAL 322
                                60.774 24.599 18.559 1.00 19.05
                                62.051 23.779 18.233 1.00 21.50
     ATOM 1256 CB VAL 322
                               62.510 22.990 19.457 1.00 21.49
     ATOM 1257 CG1 VAL 322
     ATOM 1258 CG2 VAL 322
                                61.773 22.819 17.073 1.00 15.42
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ATOM 1259 C VAL 322
                               60.947 25.375 19.867 1.00 19.89
     ATOM 1260 O VAL 322
                               60.478 24.940 20.919 1.00 21.58
                               61.591 26.537 19.788 1.00 20.25
     ATOM 1261 N LEU 323
                                61.804 27.387 20.959 1.00 19.32
     ATOM 1262 CA LEU 323
     ATOM 1263 CB LEU 323
                                62.683 28.586 20.597 1.00 12.95
 5
     ATOM 1264 CG LEU 323
                                64.129 28.273 20.217 1.00 20.70
                                64.805 29.503 19.641 1.00 13.23
     ATOM 1265 CD1 LEU 323
     ATOM 1266 CD2 LEU 323
                                64.883 27.767 21.438 1.00 22.91
     ATOM 1267 C LEU 323
                               60.468 27.884 21.497 1.00 20.25
                               60.251 27.918 22.706 1.00 25.88
     ATOM 1268 O LEU 323
10
                               59.571 28.251 20.587 1.00 23.08
     ATOM 1269 N LEU 324
                                58.248 28.753 20.944 1.00 21.24
     ATOM 1270 CA LEU 324
                                57.555 29.333 19.707 1.00 18.45
     ATOM 1271 CB LEU 324
     ATOM 1272 CG LEU 324
                                56.119 29.847 19.868 1.00 17.07
     ATOM 1273 CD1 LEU 324
                                56.083 31.092 20.752 1.00 15.39
15
     ATOM 1274 CD2 LEU 324
                                55.545 30.162 18.498 1.00 17.90
                               57.342 27.706 21.598 1.00 21.54
     ATOM 1275 C LEU 324
                               56.742 27.967 22.642 1.00 23.41
     ATOM 1276 O LEU 324
     ATOM 1277 N MET 325
                               57.249 26.521 21.003 1.00 24.63
     ATOM 1278 CA MET 325
                                56.380 25.476 21.545 1.00 25.35
20
     ATOM 1279 CB MET 325
                                55.901 24.536 20.430 1.00 25.53
     ATOM 1280 CG MET 325
                                55.235 25.220 19.232 1.00 21.89
                                53.871 26.337 19.649 1.00 25.50
     ATOM 1281 SD MET 325
                                52.705 25.250 20.397 1.00 17.66
     ATOM 1282 CE MET 325
     ATOM 1283 C MET 325
                               57.031 24.676 22.675 1.00 27.58
25
                               56.988 23.450 22.690 1.00 28.61
     ATOM 1284 O MET 325
                               57.613 25.376 23.638 1.00 27.98
     ATOM 1285 N SER 326
                                58.265 24.718 24.757 1.00 31.60
     ATOM 1286 CA SER 326
     ATOM 1287 CB SER 326
                                59.527 25.493 25.155 1.00 35.80
                                60.123 24.966 26.327 1.00 43.74
     ATOM 1288 OG SER 326
30
                               57.313 24.624 25.939 1.00 32.12
     ATOM 1289 C SER 326
     ATOM 1290 O SER 326
                               56.590 25.574 26.240 1.00 30.91
                               57.276 23.464 26.583 1.00 35.41
     ATOM 1291 N THR 327
                                56.420 23.278 27.747 1.00 39.61
     ATOM 1292 CA THR 327
                                55.777 21.890 27.758 1.00 38.84
     ATOM 1293 CB THR 327
35
                                 56.784 20.890 27.538 1.00 42.53
     ATOM 1294 OG1 THR 327
                                 54.716 21.802 26.679 1.00 40.78
     ATOM 1295 CG2 THR 327
                               57.232 23.471 29.022 1.00 43.86
     ATOM 1296 C THR 327
     ATOM 1297 O THR 327
                               56.785 23.133 30.118 1.00 42.40
                               58.417 24.054 28.869 1.00 47.35
     ATOM 1298 N ASP 328
40
     ATOM 1299 CA ASP 328
                                59.309 24.308 29.987 1.00 49.43
                                60.750 24.358 29.482 1.00 58.03
     ATOM 1300 CB ASP 328
     ATOM 1301 CG ASP 328
                                61.718 23.687 30.425 1.00 72.16
     ATOM 1302 OD1 ASP 328
                                61.816 24.117 31.595 1.00 82.32
                                62.378 22.720 29.994 1.00 81.63
     ATOM 1303 OD2 ASP 328
45
                               58.951 25.625 30.676 1.00 47.99
     ATOM 1304 C ASP 328
                               59.830 26.373 31.093 1.00 53.33
     ATOM 1305 O ASP 328
     ATOM 1306 N ARG 329
                                57.657 25.910 30.780 1.00 48.33
                               57.177 27.135 31.413 1.00 47.67
     ATOM 1307 CA ARG 329
     ATOM 1308 CB ARG 329
                                56.562 28.091 30.379 1.00 47.64
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57.550 28.802 29.450 1.00 47.87
    ATOM 1309 CG ARG 329
    ATOM 1310 CD ARG 329
                               57.893 27.968 28.226 1.00 44.00
                               58.759 28.682 27.288 1.00 41.17
    ATOM 1311 NE ARG 329
                               60.087 28.605 27.283 1.00 48.58
    ATOM 1312 CZ ARG 329
                                60.719 27.848 28.172 1.00 52.94
    ATOM 1313 NH1 ARG 329
                                60.784 29.257 26.362 1.00 43.16
    ATOM 1314 NH2 ARG 329
                              56.126 26.778 32.457 1.00 48.01
    ATOM 1315 C ARG 329
    ATOM 1316 O ARG 329
                               55.573 25.677 32.437 1.00 50.22
                              55.832 27.716 33.351 1.00 47.37
    ATOM 1317 N SER 330
                              54.848 27.490 34.402 1.00 47.64
    ATOM 1318 CA SER 330
10
                              55.376 28.021 35.736 1.00 46.62
    ATOM 1319 CB SER 330
                              53.506 28.139 34.074 1.00 46.40
    ATOM 1320 C SER 330
                              53.460 29.252 33.548 1.00 48.49
    ATOM 1321 O SER 330
    ATOM 1322 N GLY 331
                              52.421 27.424 34.359 1.00 44.16
                             51.090 27.956 34.123 1.00 41.44
    ATOM 1323 CA GLY 331
15
    ATOM 1324 C GLY 331
                              50.424 27.660 32.790 1.00 42.83
    ATOM 1325 O GLY 331
                              49.478 28.351 32.413 1.00 45.88
                              50.889 26.643 32.075 1.00 40.10
    ATOM 1326 N LEU 332
    ATOM 1327 CA LEU 332
                               50.288 26.300 30.789 1.00 39.27
    ATOM 1328 CB LEU 332
                               51.301 25.596 29.885 1.00 37.42
20
                               52.436 26.426 29.291 1.00 35.35
    ATOM 1329 CG LEU 332
                              53.374 25.505 28.530 1.00 31.61
    ATOM 1330 CD1 LEU 332
    ATOM 1331 CD2 LEU 332
                                51.875 27.511 28.376 1.00 31.82
                              49.058 25.415 30.951 1.00 39.32
    ATOM 1332 C LEU 332
                              49.060 24.467 31.738 1.00 42.74
25
    ATOM 1333 O LEU 332
                              48.009 25.730 30.202 1.00 37.62
    ATOM 1334 N LEU 333
                              46.778 24.953 30.241 1.00 41.30
    ATOM 1335 CA LEU 333
                               45.586 25.835 29.852 1.00 43.52
    ATOM 1336 CB LEU 333
                               45.125 26.904 30.848 1.00 49.39
    ATOM 1337 CG LEU 333
                               44.296 27.970 30.142 1.00 46.19
    ATOM 1338 CD1 LEU 333
30
    ATOM 1339 CD2 LEU 333
                               44.330 26.248 31.968 1.00 51.29
    ATOM 1340 C LEU 333
                              46.859 23.762 29.285 1.00 41.39
                              46.565 22.628 29.657 1.00 43.41
    ATOM 1341 O LEU 333
                               47.317 24.024 28.067 1.00 42.18
    ATOM 1342 N CYA 334
    ATOM 1343 CA CYA 334
                               47.409 23.003 27.029 1.00 39.56
35
                               47.004 23.616 25.691 1.00 45.48
    ATOM 1344 CB CYA 334
                               45.517 24.616 25.785 1.00 51.57
    ATOM 1345 SG CYA 334
                               44.187 22.808 25.555 1.00 90.90
    ATOM 1346 AS CYA 334
    ATOM 1347 C CYA 334
                               48,776 22.347 26.891 1.00 38.28
                               49.273 22.178 25.778 1.00 40.95
    ATOM 1348 O CYA 334
40
    ATOM 1349 N VAL 335
                               49.345 21.913 28.009 1.00 36.05
                               50.661 21.278 28.006 1.00 35.78
    ATOM 1350 CA VAL 335
                               50.996 20.679 29.399 1.00 35.53
    ATOM 1351 CB VAL 335
                               52.413 20.123 29.407 1.00 32.76
    ATOM 1352 CG1 VAL 335
    ATOM 1353 CG2 VAL 335
                               50.822 21.729 30.490 1.00 28.87
45
                               50.776 20.170 26.950 1.00 36.41
    ATOM 1354 C VAL 335
                               51.756 20.104 26.202 1.00 34.26
    ATOM 1355 O VAL 335
                              49.756 19.323 26.880 1.00 38.42
    ATOM 1356 N ASP 336
    ATOM 1357 CA ASP 336 49.736 18.209 25.942 1.00 39.71
    ATOM 1358 CB ASP 336 48.485 17.359 26.179 1.00 51.53
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48.534 16.028 25.452 1.00 65.98
    ATOM 1359 CG ASP 336
    ATOM 1360 OD1 ASP 336
                                49.240 15.114 25.934 1.00 70.75
                                47.858 15.891 24.406 1.00 72.15
    ATOM 1361 OD2 ASP 336
                               49.794 18.668 24.486 1.00 37.72
    ATOM 1362 C ASP 336
    ATOM 1363 O ASP 336
                               50.686 18.259 23.733 1.00 32.08
    ATOM 1364 N LYS 337
                               48.858 19.532 24.100 1.00 33.78
                                48.797 20.040 22.731 1.00 28.00
     ATOM 1365 CA LYS 337
                                47.626 21.022 22.574 1.00 22.46
    ATOM 1366 CB LYS 337
                               50.116 20.704 22.334 1.00 29.06
     ATOM 1367 C LYS 337
    ATOM 1368 O LYS 337
                               50.607 20.512 21.220 1.00 28.41
10
     ATOM 1369 N ILE 338
                              50,705 21.449 23.267 1.00 27.56
                               51.964 22.138 23.022 1.00 25.03
     ATOM 1370 CA ILE 338
                               52.274 23.149 24.144 1.00 19.49
     ATOM 1371 CB ILE 338
                                53.577 23.876 23.859 1.00 19.00
     ATOM 1372 CG2 ILE 338
                                51.135 24.167 24.232 1.00 21.97
     ATOM 1373 CG1 ILE 338
15
                                51.277 25.175 25.348 1.00 26.67
     ATOM 1374 CD1 ILE 338
                              53.119 21.153 22.826 1.00 29.97
     ATOM 1375 C ILE 338
                              53.935 21.328 21.914 1.00 31.00
     ATOM 1376 O ILE 338
                               53.165 20.100 23.642 1.00 33.52
     ATOM 1377 N GLU 339
                                54.213 19.080 23.516 1.00 35.34
     ATOM 1378 CA GLU 339
20
                                54.136 18.062 24.659 1.00 39.97
     ATOM 1379 CB GLU 339
                                54.653 18.585 25.986 1.00 53.23
     ATOM 1380 CG GLU 339
     ATOM 1381 CD GLU 339
                                54.549 17.579 27.126 1.00 61.16
                                 53.602 16.759 27.131 1.00 64.30
     ATOM 1382 OE1 GLU 339
                                 55.412 17.622 28.031 1.00 57.76
25
     ATOM 1383 OE2 GLU 339
     ATOM 1384 C GLU 339
                               54.091 18.353 22.178 1.00 31.63
                               55.086 18.123 21.491 1.00 28.96
     ATOM 1385 O GLU 339
                               52.861 18.006 21.810 1.00 30.95
     ATOM 1386 N LYS 340
     ATOM 1387 CA LYS 340
                                52.602 17.313 20.554 1.00 31.58
                                51.121 16.966 20.438 1.00 31.83
     ATOM 1388 CB LYS 340
30
                               53.057 18.159 19.358 1.00 29.84
     ATOM 1389 C LYS 340
                               53.696 17.640 18.438 1.00 31.58
     ATOM 1390 O LYS 340
                               52.765 19.460 19.388 1.00 25.33
     ATOM 1391 N SER 341
                                53.165 20.351 18.297 1.00 23.92
     ATOM 1392 CA SER 341
                                52.468 21.707 18.400 1.00 24.02
     ATOM 1393 CB SER 341
35
                                52,700 22,302 19,657 1,00 48,88
     ATOM 1394 OG SER 341
                               54.677 20.533 18.240 1.00 24.39
     ATOM 1395 C SER 341
                               55.254 20.593 17.150 1.00 24.71
     ATOM 1396 O SER 341
                               55.324 20.606 19.405 1.00 25.45
     ATOM 1397 N GLN 342
                                56.777 20.751 19.437 1.00 26.66
40
     ATOM 1398 CA GLN 342
     ATOM 1399 CB GLN 342
                                57.311 20.975 20.853 1.00 22.77
     ATOM 1400 CG GLN 342
                                 58.805 21.307 20.840 1.00 25.76
                                 59.427 21.371 22.214 1.00 28.46
     ATOM 1401 CD GLN 342
                                 59.342 20.422 22.990 1.00 34.22
     ATOM 1402 OE1 GLN 342
     ATOM 1403 NE2 GLN 342
                                 60.080 22.483 22.517 1.00 30.01
45
                                57.425 19.504 18.843 1.00 23.37
     ATOM 1404 C GLN 342
                                58.414 19.598 18.106 1.00 23.65
     ATOM 1405 O GLN 342
                                56.864 18.340 19.162 1.00 21.48
     ATOM 1406 N GLU 343
                               57.370 17.076 18.641 1.00 20.74
     ATOM 1407 CA GLU 343
                                56.599 15.902 19.247 1.00 22.09
50
     ATOM 1408 CB GLU 343
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57.225 17.094 17.119 1.00 19.18
    ATOM 1409 C GLU 343
                               58.156 16.743 16.393 1.00 21.11
    ATOM 1410 O GLU 343
                               56.077 17.570 16.648 1.00 19.93
    ATOM 1411 N ALA 344
                                55.803 17.662 15.217 1.00 20.20
    ATOM 1412 CA ALA 344
    ATOM 1413 CB ALA 344
                                54.411 18.216 14.989 1.00 16.46
5
    ATOM 1414 C ALA 344
                               56.850 18.539 14.528 1.00 20.75
                               57.432 18.140 13.514 1.00 25.13
    ATOM 1415 O ALA 344
                               57.105 19.722 15.088 1.00 21.31
    ATOM 1416 N TYR 345
                                58.107 20.631 14.531 1.00 15.93
    ATOM 1417 CA TYR 345
    ATOM 1418 CB TYR 345
                                58.127 21.969 15.282 1.00 17.29
10
                                57.049 22.927 14.833 1.00 16.11
    ATOM 1419 CG TYR 345
    ATOM 1420 CD1 TYR 345
                                56.017 23.296 15.689 1.00 9.93
    ATOM 1421 CE1 TYR 345
                                54.999 24.138 15.263 1.00 16.95
                                57.041 23.431 13.531 1.00 19.84
    ATOM 1422 CD2 TYR 345
    ATOM 1423 CE2 TYR 345
                                56.026 24.276 13.094 1.00 17.13
15
                                55.005 24.622 13.963 1.00 18.12
    ATOM 1424 CZ TYR 345
                                53.980 25.430 13.530 1.00 26.25
    ATOM 1425 OH TYR 345
                               59.493 20.008 14.554 1.00 20.65
    ATOM 1426 C TYR 345
    ATOM 1427 O TYR 345
                               60.240 20.129 13.583 1.00 20.75
                               59.832 19.337 15.655 1.00 22.14
20
    ATOM 1428 N LEU 346
                                61.134 18.684 15.803 1.00 19.43
    ATOM 1429 CA LEU 346
    ATOM 1430 CB LEU 346
                                61.267 18.041 17.186 1.00 19.92
                                61.683 18.945 18.347 1.00 25.56
    ATOM 1431 CG LEU 346
                                61.440 18.244 19.677 1.00 22.06
    ATOM 1432 CD1 LEU 346
    ATOM 1433 CD2 LEU 346
                                63.147 19.332 18.197 1.00 17.62
25
                               61.359 17.635 14.723 1.00 19.30
    ATOM 1434 C LEU 346
                               62.441 17.560 14.142 1.00 22.84
    ATOM 1435 O LEU 346
                               60.337 16.826 14.456 1.00 25.17
     ATOM 1436 N LEU 347
     ATOM 1437 CA LEU 347
                                60.423 15.790 13.427 1.00 24.55
                                59.187 14.892 13.453 1.00 25.47
     ATOM 1438 CB LEU 347
30
                                59.256 13.654 14.345 1.00 30.65
     ATOM 1439 CG LEU 347
                                57.941 12.890 14.258 1.00 34.28
     ATOM 1440 CD1 LEU 347
     ATOM 1441 CD2 LEU 347
                                60.416 12.765 13.908 1.00 28.26
                               60.584 16.400 12.042 1.00 24.00
     ATOM 1442 C LEU 347
     ATOM 1443 O LEU 347
                               61.399 15.932 11.245 1.00 29.74
35
                               59.809 17.443 11.761 1.00 22.72
     ATOM 1444 N ALA 348
                                59.875 18.125 10.475 1.00 19.19
     ATOM 1445 CA ALA 348
                                58.789 19.188 10.388 1.00 22.73
     ATOM 1446 CB ALA 348
                               61.246 18.762 10.316 1.00 20.34
     ATOM 1447 C ALA 348
                               61.881 18.633 9.274 1.00 23.94
     ATOM 1448 O ALA 348
40
                               61.707 19.402 11.388 1.00 22.19
     ATOM 1449 N PHE 349
     ATOM 1450 CA PHE 349
                                63.001 20.078 11.435 1.00 19.41
                                63.185 20.701 12.832 1.00 17.45
     ATOM 1451 CB PHE 349
                                64.371 21.632 12.963 1.00 18.70
     ATOM 1452 CG PHE 349
                                65.183 21.943 11.874 1.00 19.09
     ATOM 1453 CD1 PHE 349
45
                                64.669 22.203 14.199 1.00 21.81
     ATOM 1454 CD2 PHE 349
     ATOM 1455 CE1 PHE 349
                                66.270 22.811 12.012 1.00 21.49
                                65.753 23.072 14.351 1.00 18.58
     ATOM 1456 CE2 PHE 349
                                66.555 23.376 13.256 1.00 18.67
     ATOM 1457 CZ PHE 349
                               64.110 19.071 11.136 1.00 20.96
     ATOM 1458 C PHE 349
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64.967 19.311 10.283 1.00 25.19
    ATOM 1459 O PHE 349
                               64.076 17.935 11.824 1.00 23.96
    ATOM 1460 N GLU 350
                                65.077 16.888 11.642 1.00 27.98
    ATOM 1461 CA GLU 350
                                64.794 15.721 12.591 1.00 28.90
    ATOM 1462 CB GLU 350
    ATOM 1463 CG GLU 350
                                65.738 14.542 12.413 1.00 39.36
5
    ATOM 1464 CD GLU 350
                                65.603 13.497 13.505 1.00 41.62
                                64.475 13.260 13.988 1.00 43.67
    ATOM 1465 OE1 GLU 350
                                66.636 12.908 13.876 1.00 49.64
    ATOM 1466 OE2 GLU 350
    ATOM 1467 C GLU 350
                               65.100 16.385 10.203 1.00 27.12
                               66.158 16.288 9.577 1.00 27.44
    ATOM 1468 O GLU 350
10
                              63.918 16.088 9.678 1.00 27.36
    ATOM 1469 N HIS 351
                               63.787 15.591 8.318 1.00 23.97
    ATOM 1470 CA HIS 351
    ATOM 1471 CB HIS 351
                               62.366 15.087 8.090 1.00 22.89
                               61.991 13.945 8.986 1.00 24.58
    ATOM 1472 CG HIS 351
                               62.736 13.209 9.846 1.00 25.83
    ATOM 1473 CD2 HIS 351
15
                               60.709 13.448 9.073 1.00 26.50
    ATOM 1474 ND1 HIS 351
                               60.677 12.460 9.948 1.00 24.81
    ATOM 1475 CE1 HIS 351
                               61.896 12.295 10.431 1.00 28.42
    ATOM 1476 NE2 HIS 351
                              64.200 16.635 7.278 1.00 24.22
    ATOM 1477 C HIS 351
                              64.757 16.287 6.236 1.00 25.79
20
    ATOM 1478 O HIS 351
                               63.969 17.912 7.572 1.00 21.04
    ATOM 1479 N TYR 352
                                64.363 18.974 6.654 1.00 18.98
    ATOM 1480 CA TYR 352
                                63.770 20.321 7.067 1.00 17.08
    ATOM 1481 CB TYR 352
                                64.127 21.413 6.090 1.00 21.83
    ATOM 1482 CG TYR 352
    ATOM 1483 CD1 TYR 352
                                63.537 21.467 4.828 1.00 20.07
25
                                63.941 22.411 3.883 1.00 23.51
    ATOM 1484 CE1 TYR 352
                                65.121 22.339 6.388 1.00 19.94
    ATOM 1485 CD2 TYR 352
    ATOM 1486 CE2 TYR 352
                                65.531 23.284 5.452 1.00 20.85
    ATOM 1487 CZ TYR 352
                                64.942 23.313 4.203 1.00 24.80
                                65.380 24.221 3.269 1.00 26.74
    ATOM 1488 OH TYR 352
30
                               65.889 19.055 6.624 1.00 20.58
    ATOM 1489 C TYR 352
    ATOM 1490 O TYR 352
                               66.492 19.276 5.570 1.00 22.72
                               66.508 18.877 7.789 1.00 28.34
     ATOM 1491 N VAL 353
                                67.967 18.892 7.904 1.00 22.38
    ATOM 1492 CA VAL 353
                                68.419 18.755 9.389 1.00 26.46
    ATOM 1493 CB VAL 353
35
                                69.915 18.527 9.478 1.00 20.92
    ATOM 1494 CG1 VAL 353
     ATOM 1495 CG2 VAL 353
                                68.053 20.009 10.165 1.00 22.46
                               68.518 17.725 7.078 1.00 23.51
     ATOM 1496 C VAL 353
                               69.535 17.865 6.391 1.00 24.73
     ATOM 1497 O VAL 353
                               67.850 16.575 7.158 1.00 20.93
     ATOM 1498 N ASN 354
40
                                68.252 15.392 6.397 1.00 27.25
     ATOM 1499 CA ASN 354
     ATOM 1500 CB ASN 354
                                67.320 14.210 6.680 1.00 28.43
                                67.521 13.607 8.058 1.00 31.50
     ATOM 1501 CG ASN 354
     ATOM 1502 OD1 ASN 354
                                68.565 13.787 8.692 1.00 37.79
     ATOM 1503 ND2 ASN 354
                                66.521 12.867 8.524 1.00 26.44
45
                               68.182 15.721 4.908 1.00 31.27
     ATOM 1504 C ASN 354
                               69.066 15.347 4.134 1.00 34.22
     ATOM 1505 O ASN 354
     ATOM 1506 N HIS 355
                              67.124 16.429 4.520 1.00 30.49
                               66,917 16.826 3.132 1.00 26.88
     ATOM 1507 CA HIS 355
                               65.548 17.494 2.975 1.00 27.27
    ATOM 1508 CB HIS 355
50
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65.319 18.103 1.625 1.00 37.76
    ATOM 1509 CG HIS 355
                               65.439 19.382 1.196 1.00 35.28
    ATOM 1510 CD2 HIS 355
                               64.913 17.369 0.532 1.00 34.93
    ATOM 1511 ND1 HIS 355
                               64.789 18.169 -0.513 1.00 34.84
    ATOM 1512 CE1 HIS 355
    ATOM 1513 NE2 HIS 355
                               65.104 19.394 -0.135 1.00 33.13
5
                              68.016 17.748 2.610 1.00 24.66
    ATOM 1514 C HIS 355
                              68.420 17.630 1.456 1.00 26.62
    ATOM 1515 O HIS 355
                               68.487 18.670 3.448 1.00 25.86
    ATOM 1516 N ARG 356
    ATOM 1517 CA ARG 356
                                69.536 19.608 3.040 1.00 26.94
                                69.620 20.791 3.996 1.00 20.57
    ATOM 1518 CB ARG 356
10
                                68.453 21.727 3.899 1.00 19.69
    ATOM 1519 CG ARG 356
                                68.866 23.110 4.340 1.00 23.81
    ATOM 1520 CD ARG 356
    ATOM 1521 NE ARG 356
                                69.768 23.746 3.388 1.00 23.14
                                70.641 24.697 3.702 1.00 24.11
    ATOM 1522 CZ ARG 356
                                70.755 25.129 4.949 1.00 26.29
    ATOM 1523 NH1 ARG 356
15
    ATOM 1524 NH2 ARG 356
                                71.384 25.242 2.754 1.00 32.79
                               70.921 19.002 2.875 1.00 29.38
    ATOM 1525 C ARG 356
                               71.795 19.607 2.257 1.00 32.91
    ATOM 1526 O ARG 356
                               71.133 17.848 3.498 1.00 33.39
    ATOM 1527 N LYS 357
                                72.401 17.128 3.417 1.00 35.97
    ATOM 1528 CA LYS 357
20
                                72.479 16.363 2.089 1.00 40.55
    ATOM 1529 CB LYS 357
    ATOM 1530 CG LYS 357
                                71.327 15.381 1.891 1.00 44.03
                                71.360 14.722 0.523 1.00 52.31
     ATOM 1531 CD LYS 357
                                70.171 13.787 0.343 1.00 56.99
     ATOM 1532 CE LYS 357
     ATOM 1533 NZ LYS 357
                                70.208 13.085 -0.970 1.00 64.78
25
                               73.657 17.981 3.629 1.00 38.55
     ATOM 1534 C LYS 357
                               74.518 18.079 2.748 1.00 42.50
     ATOM 1535 O LYS 357
                               73.751 18.601 4.802 1.00 35.00
     ATOM 1536 N HIS 358
                               74.906 19.418 5.155 1.00 32.94
     ATOM 1537 CA HIS 358
                               74.732 20.018 6.552 1.00 27.62
     ATOM 1538 CB HIS 358
30
                               73.669 21.067 6.643 1.00 26.64
     ATOM 1539 CG HIS 358
                                72.330 20.968 6.819 1.00 20.85
     ATOM 1540 CD2 HIS 358
                                73.950 22.416 6.587 1.00 24.71
     ATOM 1541 ND1 HIS 358
                                72.831 23.103 6.724 1.00 21.02
     ATOM 1542 CE1 HIS 358
                                71.834 22.248 6.865 1.00 21.42
     ATOM 1543 NE2 HIS 358
35
                               76.140 18.520 5.176 1.00 36.60
     ATOM 1544 C HIS 358
                               76.072 17.379 5.635 1.00 38.73
     ATOM 1545 O HIS 358
                               77.267 19.037 4.702 1.00 41.40
     ATOM 1546 N ASN 359
                                78.515 18.277 4.689 1.00 45.02
     ATOM 1547 CA ASN 359
                                79.441 18.799 3.587 1.00 42.57
     ATOM 1548 CB ASN 359
40
                               79.193 18.386 6.058 1.00 46.59
     ATOM 1549 C ASN 359
                               80.405 18.588 6.150 1.00 52.31
     ATOM 1550 O ASN 359
                               78.400 18.254 7.117 1.00 45.14
     ATOM 1551 N ILE 360
                               78.896 18.348 8.487 1.00 43.69
     ATOM 1552 CA ILE 360
                               78.330 19.597 9.207 1.00 40.08
     ATOM 1553 CB ILE 360
45
                                78.824 19.657 10.645 1.00 32.11
     ATOM 1554 CG2 ILE 360
                                78.733 20.864 8.452 1.00 41.47
     ATOM 1555 CG1 ILE 360
     ATOM 1556 CD1 ILE 360
                               78.057 22.115 8.954 1.00 44.93
                              78.452 17.101 9.242 1.00 43.63
     ATOM 1557 C ILE 360
                              77.257 16.797 9.313 1.00 45.20
     ATOM 1558 O ILE 360
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79.413 16.337 9.780 1.00 43.91
    ATOM 1559 N PRO 361
                                80.871 16.540 9.699 1.00 47.07
    ATOM 1560 CD PRO 361
                                79.087 15.118 10.526 1.00 41.66
    ATOM 1561 CA PRO 361
                                80.462 14.495 10.782 1.00 43.73
    ATOM 1562 CB PRO 361
                                81.383 15.679 10.830 1.00 45.45
    ATOM 1563 CG PRO 361
                               78.332 15.403 11.832 1.00 36.42
    ATOM 1564 C PRO 361
    ATOM 1565 O PRO 361
                               78.679 16.325 12.572 1.00 35.74
                              77.291 14.610 12.088 1.00 33.14
    ATOM 1566 N HIS 362
                               76.462 14.726 13.292 1.00 34.09
    ATOM 1567 CA HIS 362
    ATOM 1568 CB HIS 362
                               77.288 14.413 14.547 1.00 33.82
10
                               78.132 13.181 14.424 1.00 36.04
    ATOM 1569 CG HIS 362
                                77.793 11.885 14.224 1.00 34.77
    ATOM 1570 CD2 HIS 362
     ATOM 1571 ND1 HIS 362
                                79.509 13.212 14.482 1.00 37.16
    ATOM 1572 CE1 HIS 362
                               79.983 11.990 14.325 1.00 37.16
                                78.962 11.165 14.167 1.00 40.13
    ATOM 1573 NE2 HIS 362
15
    ATOM 1574 C HIS 362
                              75.829 16.110 13.417 1.00 31.00
                              75.617 16.608 14.525 1.00 30.22
     ATOM 1575 O HIS 362
     ATOM 1576 N PHE 363
                               75.478 16.690 12.272 1.00 33.06
     ATOM 1577 CA PHE 363
                                74.878 18.021 12.200 1.00 28.08
                                74.503 18.355 10.747 1.00 25.26
     ATOM 1578 CB PHE 363
20
                                73.923 19.733 10.567 1.00 24.91
     ATOM 1579 CG PHE 363
    ATOM 1580 CD1 PHE 363
                                74.750 20.817 10.320 1.00 27.60
     ATOM 1581 CD2 PHE 363
                                72.552 19.948 10.664 1.00 25.52
                                74.221 22.100 10.175 1.00 29.70
     ATOM 1582 CE1 PHE 363
     ATOM 1583 CE2 PHE 363
                                72.014 21.227 10.522 1.00 25.88
25
     ATOM 1584 CZ PHE 363
                                72.850 22.304 10.278 1.00 21.49
                               73.659 18.201 13.099 1.00 23.79
     ATOM 1585 C PHE 363
                               73.587 19.164 13.863 1.00 24.48
     ATOM 1586 O PHE 363
                               72.707 17.277 13.012 1.00 23.13
     ATOM 1587 N TRP 364
                                71.484 17.369 13.805 1.00 25.06
     ATOM 1588 CA TRP 364
30
                                70.536 16.201 13.494 1.00 21.17
     ATOM 1589 CB TRP 364
                                69.247 16.220 14.271 1.00 23.14
     ATOM 1590 CG TRP 364
                                68.261 17.266 14.296 1.00 27.68
     ATOM 1591 CD2 TRP 364
     ATOM 1592 CE2 TRP 364
                                67.229 16.845 15.165 1.00 28.31
     ATOM 1593 CE3 TRP 364
                                68.149 18.517 13.671 1.00 26.46
35
     ATOM 1594 CD1 TRP 364
                                68.784 15.241 15.096 1.00 23.76
     ATOM 1595 NE1 TRP 364
                                67.576 15.607 15.637 1.00 32.12
                                66.100 17.628 15.427 1.00 25.63
     ATOM 1596 CZ2 TRP 364
     ATOM 1597 CZ3 TRP 364
                                67.028 19.294 13.931 1.00 25.55
                                66.017 18.845 14.803 1.00 29.79
     ATOM 1598 CH2 TRP 364
40
                               71.715 17.531 15.312 1.00 27.80
     ATOM 1599 C TRP 364
     ATOM 1600 O TRP 364
                               71.212 18.486 15.904 1.00 26.96
                               72.458 16.605 15.955 1.00 30.69
     ATOM 1601 N PRO 365
                                72.974 15.308 15.481 1.00 31.45
     ATOM 1602 CD PRO 365
45
     ATOM 1603 CA PRO 365
                                72.687 16.757 17.397 1.00 27.97
                                73.506 15.512 17.752 1.00 26.50
     ATOM 1604 CB PRO 365
                                73.057 14.509 16.757 1.00 33.47
     ATOM 1605 CG PRO 365
     ATOM 1606 C PRO 365
                               73.457 18.043 17.709 1.00 27.10
                               73.154 18.736 18.681 1.00 26.88
     ATOM 1607 O PRO 365
                               74.440 18.365 16.873 1.00 26.99
50
     ATOM 1608 N LYS 366
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75.230 19.577 17.061 1.00 30.69
    ATOM 1609 CA LYS 366
    ATOM 1610 CB LYS 366
                                76.275 19.708 15.957 1.00 28.53
                                77.481 18.804 16.106 1.00 28.89
    ATOM 1611 CG LYS 366
                                78.430 19.027 14.939 1.00 32.51
    ATOM 1612 CD LYS 366
                               79.743 18.294 15.116 1.00 38.52
    ATOM 1613 CE LYS 366
 5
    ATOM 1614 NZ LYS 366
                               80.632 18.506 13.939 1.00 45.28
                               74.349 20.831 17.079 1.00 36.18
    ATOM 1615 C LYS 366
                               74.472 21.672 17.972 1.00 39.82
    ATOM 1616 O LYS 366
                               73.464 20.950 16.091 1.00 37.54
    ATOM 1617 N LEU 367
    ATOM 1618 CA LEU 367
                                72.557 22.092 15.994 1.00 36.14
10
                                71.803 22.070 14.659 1.00 32.20
    ATOM 1619 CB LEU 367
                                70.764 23.179 14.447 1.00 36.16
    ATOM 1620 CG LEU 367
                                71.402 24.567 14.618 1.00 20.60
    ATOM 1621 CD1 LEU 367
     ATOM 1622 CD2 LEU 367
                                70.139 23.030 13.065 1.00 34.30
    ATOM 1623 C LEU 367
                               71.561 22.060 17.143 1.00 36.84
15
                               71.231 23.091 17.729 1.00 36.94
     ATOM 1624 O LEU 367
                               71.083 20.866 17.459 1.00 37.81
     ATOM 1625 N LEU 368
                                70.130 20.683 18.536 1.00 34.83
     ATOM 1626 CA LEU 368
                                69.763 19.205 18.622 1.00 36.98
     ATOM 1627 CB LEU 368
     ATOM 1628 CG LEU 368
                                68.421 18.777 19.205 1.00 40.34
20
                                67.276 19.595 18.619 1.00 36.28
     ATOM 1629 CD1 LEU 368
                                68.241 17.299 18.908 1.00 39.39
     ATOM 1630 CD2 LEU 368
                               70.755 21.182 19.843 1.00 38.32
     ATOM 1631 C LEU 368
                               70.059 21.711 20.707 1.00 41.87
     ATOM 1632 O LEU 368
                               72.075 21.057 19.962 1.00 39.46
     ATOM 1633 N MET 369
25
                                72.790 21.515 21.154 1.00 40.12
     ATOM 1634 CA MET 369
                                74.219 20.971 21.168 1.00 41.26
     ATOM 1635 CB MET 369
     ATOM 1636 CG MET 369
                                74.307 19.493 21.521 1.00 47.83
     ATOM 1637 SD MET 369
                                75.961 18.810 21.289 1.00 55.72
     ATOM 1638 CE MET 369
                                76.809 19.474 22.727 1.00 54.37
30
                               72.805 23.039 21.251 1.00 42.81
     ATOM 1639 C MET 369
                               72.990 23.601 22.335 1.00 47.81
     ATOM 1640 O MET 369
     ATOM 1641 N LYS 370
                               72.622 23.708 20.115 1.00 40.09
                                72.588 25.165 20.080 1.00 33.65
     ATOM 1642 CA LYS 370
                                72.751 25.677 18.650 1.00 30.83
     ATOM 1643 CB LYS 370
35
                                74.138 25.435 18.078 1.00 30.98
     ATOM 1644 CG LYS 370
                                75.188 26.198 18.867 1.00 37.82
     ATOM 1645 CD LYS 370
                                76.591 25.938 18.351 1.00 36.05
     ATOM 1646 CE LYS 370
                                77.034 24.562 18.667 1.00 48.68
     ATOM 1647 NZ LYS 370
     ATOM 1648 C LYS 370
                               71.293 25.684 20.702 1.00 33.32
40
                               71.218 26.842 21.112 1.00 34.75
     ATOM 1649 O LYS 370
                               70.277 24.826 20.779 1.00 31.90
     ATOM 1650 N VAL 371
     ATOM 1651 CA VAL 371
                                69.006 25.197 21.395 1.00 31.77
                                67.933 24.092 21.214 1.00 30.28
     ATOM 1652 CB VAL 371
45
     ATOM 1653 CG1 VAL 371
                                 66.673 24.429 21.995 1.00 30.02
                                 67.596 23.933 19.746 1.00 32.23
     ATOM 1654 CG2 VAL 371
                               69.277 25.417 22.885 1.00 34.44
     ATOM 1655 C VAL 371
                               68.722 26.331 23.499 1.00 33.35
     ATOM 1656 O VAL 371
                               70.161 24.590 23.443 1.00 33.15
     ATOM 1657 N THR 372
                               70.551 24.675 24.847 1.00 32.47
     ATOM 1658 CA THR 372
50
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71.541 23.556 25.207 1.00 32.11
    ATOM 1659 CB THR 372
                                70.955 22.288 24.891 1.00 35.33
    ATOM 1660 OG1 THR 372
                                71.894 23.603 26.688 1.00 32.54
    ATOM 1661 CG2 THR 372
    ATOM 1662 C THR 372
                               71.226 26.020 25.108 1.00 34.49
                               70.936 26.696 26.099 1.00 34.07
    ATOM 1663 O THR 372
                               72.120 26.405 24.202 1.00 32.77
    ATOM 1664 N ASP 373
                               72.830 27.671 24.315 1.00 28.08
    ATOM 1665 CA ASP 373
    ATOM 1666 CB ASP 373
                               73.803 27.841 23.147 1.00 31.59
                                74.910 26.789 23.142 1.00 37.29
    ATOM 1667 CG ASP 373
    ATOM 1668 OD1 ASP 373
                                75.170 26.169 24.196 1.00 40.82
10
                                75.531 26.586 22.079 1.00 40.81
    ATOM 1669 OD2 ASP 373
                               71.830 28.821 24.353 1.00 29.21
    ATOM 1670 C ASP 373
                               71.931 29.709 25.200 1.00 31.85
    ATOM 1671 O ASP 373
                               70.843 28.775 23.463 1.00 24.71
    ATOM 1672 N LEU 374
                                69.813 29.802 23.403 1.00 25.25
    ATOM 1673 CA LEU 374
15
                                68.906 29.587 22.188 1.00 25.61
    ATOM 1674 CB LEU 374
                                69.480 30.084 20.858 1.00 25.51
    ATOM 1675 CG LEU 374
    ATOM 1676 CD1 LEU 374
                                68.741 29.469 19.677 1.00 23.53
                                69.405 31.596 20.820 1.00 21.92
    ATOM 1677 CD2 LEU 374
    ATOM 1678 C LEU 374
                               68.994 29.827 24.686 1.00 26.84
20
                               68.591 30.895 25.151 1.00 28.96
    ATOM 1679 O LEU 374
    ATOM 1680 N ARG 375
                               68.746 28.651 25.254 1.00 31.00
                                67.996 28.554 26.502 1.00 32.86
    ATOM 1681 CA ARG 375
    ATOM 1682 CB ARG 375
                                67.831 27.090 26.924 1.00 36.80
                                66.861 26.297 26.071 1.00 44.91
    ATOM 1683 CG ARG 375
25
                                65.433 26.731 26.338 1.00 58.99
    ATOM 1684 CD ARG 375
    ATOM 1685 NE ARG 375
                                64.501 26.210 25.342 1.00 72.26
                                63.909 25.020 25.404 1.00 77.46
    ATOM 1686 CZ ARG 375
                                 64.147 24.201 26.422 1.00 80.94
    ATOM 1687 NH1 ARG 375
    ATOM 1688 NH2 ARG 375
                                 63.062 24.657 24.447 1.00 75.58
30
                               68.771 29.317 27.570 1.00 32.27
     ATOM 1689 C ARG 375
                               68.199 30.125 28.304 1.00 33.75
    ATOM 1690 O ARG 375
    ATOM 1691 N MET 376
                                70.084 29.098 27.602 1.00 32.65
     ATOM 1692 CA MET 376
                                70.967 29.753 28.560 1.00 35.83
                                72.392 29.210 28.434 1.00 39.25
     ATOM 1693 CB MET 376
35
                                72.526 27.751 28.839 1.00 54.45
     ATOM 1694 CG MET 376
                                74.245 27.212 28.944 1.00 73.93
     ATOM 1695 SD MET 376
     ATOM 1696 CE MET 376
                                74.421 26.270 27.434 1.00 67.01
                               70.960 31.267 28.378 1.00 35.38
     ATOM 1697 C MET 376
     ATOM 1698 O MET 376
                                70.882 32.015 29.353 1.00 34.73
40
                               71.038 31.716 27.129 1.00 32.51
     ATOM 1699 N ILE 377
                               71.016 33.142 26.816 1.00 26.55
     ATOM 1700 CA ILE 377
     ATOM 1701 CB ILE 377
                               71.182 33.370 25.299 1.00 24.84
                                70.817 34.797 24.923 1.00 26.63
     ATOM 1702 CG2 ILE 377
45
     ATOM 1703 CG1 ILE 377
                                72.616 33.038 24.890 1.00 20.66
     ATOM 1704 CD1 ILE 377
                                72.872 33.104 23.409 1.00 20.74
                              69.706 33.755 27.313 1.00 25.47
     ATOM 1705 C ILE 377
                              69.696 34.848 27.881 1.00 29.99
     ATOM 1706 O ILE 377
     ATOM 1707 N GLY 378
                               68.608 33.033 27.127 1.00 25.11
                               67.321 33.522 27.580 1.00 27.82
     ATOM 1708 CA GLY 378
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67.279 33.613 29.095 1.00 30.90
    ATOM 1709 C GLY 378
    ATOM 1710 O GLY 378
                               66.749 34.579 29.651 1.00 31.19
                               67.851 32.611 29.761 1.00 31.62
    ATOM 1711 N ALA 379
                               67.896 32.547 31.223 1.00 30.74
    ATOM 1712 CA ALA 379
                                68.433 31.198 31.671 1.00 30.82
    ATOM 1713 CB ALA 379
                               68.756 33.668 31.801 1.00 30.07
    ATOM 1714 C ALA 379
                               68.327 34.384 32.708 1.00 31.05
    ATOM 1715 O ALA 379
                               69.966 33.817 31.273 1.00 29.72
    ATOM 1716 N CYA 380
                                70.873 34.866 31.723 1.00 33.36
    ATOM 1717 CA CYA 380
                                72.201 34.809 30.963 1.00 38.31
    ATOM 1718 CB CYA 380
10
                                73.249 33.407 31.386 1.00 50.99
    ATOM 1719 SG CYA 380
                                74.982 33.655 29.929 1.00 70.37
    ATOM 1720 AS CYA 380
                               70.226 36.232 31.535 1.00 33.40
    ATOM 1721 C CYA 380
    ATOM 1722 O CYA 380
                               70.246 37.062 32.442 1.00 36.41
                              69.615 36.456 30.374 1.00 32.55
15
    ATOM 1723 N HIS 381
                               68.965 37.734 30.114 1.00 26.41
    ATOM 1724 CA HIS 381
                               68.434 37.811 28.681 1.00 20.89
    ATOM 1725 CB HIS 381
                               67.593 39.023 28.423 1.00 15.78
     ATOM 1726 CG HIS 381
     ATOM 1727 CD2 HIS 381
                               67.928 40.277 28.041 1.00 12.67
                                66.226 39.031 28.605 1.00 17.88
    ATOM 1728 ND1 HIS 381
20
    ATOM 1729 CE1 HIS 381
                               65.756 40.239 28.353 1.00 16.27
                               66.768 41.013 28.008 1.00 17.18
    ATOM 1730 NE2 HIS 381
                              67.839 38.023 31.102 1.00 26.73
     ATOM 1731 C HIS 381
                              67.621 39.176 31.464 1.00 30.46
     ATOM 1732 O HIS 381
                               67.111 36.991 31.521 1.00 26.68
25
     ATOM 1733 N ALA 382
                                66.010 37.176 32.464 1.00 27.90
    ATOM 1734 CA ALA 382
                                65.237 35.878 32.642 1.00 25.29
     ATOM 1735 CB ALA 382
                               66.511 37.697 33.810 1.00 31.23
     ATOM 1736 C ALA 382
                               65.927 38.617 34.378 1.00 37.67
     ATOM 1737 O ALA 382
                               67.596 37.114 34.316 1.00 34.15
     ATOM 1738 N SER 383
30
                               68.174 37.550 35.588 1.00 37.23
     ATOM 1739 CA SER 383
                               69.294 36.605 36.027 1.00 40.21
     ATOM 1740 CB SER 383
     ATOM 1741 OG SER 383
                                68.785 35.324 36.361 1.00 53.99
     ATOM 1742 C SER 383
                               68.727 38.958 35.417 1.00 33.67
                               68.532 39.827 36.268 1.00 40.73
     ATOM 1743 O SER 383
35
                               69.411 39.171 34.298 1.00 29.95
     ATOM 1744 N ARG 384
                                70.000 40.458 33.957 1.00 29.77
     ATOM 1745 CA ARG 384
                                70.684 40.350 32.594 1.00 30.79
     ATOM 1746 CB ARG 384
     ATOM 1747 CG ARG 384
                                71.481 41.558 32.167 1.00 31.34
                                72.781 41.638 32.918 1.00 33.62
     ATOM 1748 CD ARG 384
40
     ATOM 1749 NE ARG 384
                                73.657 42.660 32.358 1.00 41.68
                                74,584 43.310 33.052 1.00 41.20
     ATOM 1750 CZ ARG 384
                                 74.756 43.047 34.339 1.00 42.11
     ATOM 1751 NH1 ARG 384
                                 75.349 44.213 32.455 1.00 37.27
     ATOM 1752 NH2 ARG 384
     ATOM 1753 C ARG 384
                               68.910 41.536 33.911 1.00 35.72
45
                               69.090 42.635 34.439 1.00 41.66
     ATOM 1754 O ARG 384
                               67.768 41.196 33.318 1.00 34.30
     ATOM 1755 N PHE 385
     ATOM 1756 CA PHE 385
                               66.646 42.119 33.199 1.00 32.40
                                65.527 41.502 32.356 1.00 29.02
     ATOM 1757 CB PHE 385
                                64.344 42.407 32.163 1.00 26.56
     ATOM 1758 CG PHE 385
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64.317 43.320 31.119 1.00 26.59
    ATOM 1759 CD1 PHE 385
                                63.263 42.355 33.037 1.00 24.69
    ATOM 1760 CD2 PHE 385
                                63.231 44.173 30.947 1.00 31.70
    ATOM 1761 CE1 PHE 385
    ATOM 1762 CE2 PHE 385
                               62.174 43.202 32.875 1.00 26.79
                               62.158 44.115 31.827 1.00 31.59
    ATOM 1763 CZ PHE 385
                              66.121 42.492 34.578 1.00 32.98
    ATOM 1764 C PHE 385
                               65.822 43.659 34.839 1.00 33.91
    ATOM 1765 O PHE 385
                               66.003 41.499 35.456 1.00 33.91
    ATOM 1766 N LEU 386
                               65.533 41.736 36.818 1.00 38.66
    ATOM 1767 CA LEU 386
    ATOM 1768 CB LEU 386
                               65.547 40.440 37.633 1.00 43.79
10
                               64.327 39.521 37.525 1.00 49.81
    ATOM 1769 CG LEU 386
                                64.652 38.147 38.099 1.00 51.12
    ATOM 1770 CD1 LEU 386
                                63.135 40.148 38.246 1.00 49.17
    ATOM 1771 CD2 LEU 386
    ATOM 1772 C LEU 386
                               66.445 42.761 37.475 1.00 38.95
                               65.979 43.682 38.146 1.00 42.16
    ATOM 1773 O LEU 386
15
                              67.745 42.613 37.248 1.00 33.62
    ATOM 1774 N HIS 387
    ATOM 1775 CA HIS 387
                               68.723 43.531 37.808 1.00 39.73
    ATOM 1776 CB HIS 387
                               70.138 42.980 37.639 1.00 40.71
                               70.403 41.749 38.449 1.00 52.03
    ATOM 1777 CG HIS 387
    ATOM 1778 CD2 HIS 387
                               69.573 40.967 39.181 1.00 53.85
20
                               71.657 41.189 38.566 1.00 54.79
    ATOM 1779 ND1 HIS 387
                               71.590 40.114 39.334 1.00 56.55
    ATOM 1780 CE1 HIS 387
    ATOM 1781 NE2 HIS 387
                               70.336 39.958 39.720 1.00 57.48
                              68.594 44.913 37.175 1.00 42.08
    ATOM 1782 C HIS 387
                              68.712 45.926 37.865 1.00 44.12
    ATOM 1783 O HIS 387
25
                               68.318 44.957 35.874 1.00 42.38
    ATOM 1784 N MET 388
    ATOM 1785 CA MET 388
                                68.154 46.229 35.175 1.00 38.00
                                67.840 46.006 33.692 1.00 40.21
    ATOM 1786 CB MET 388
                                69.009 45.555 32.829 1.00 41.26
    ATOM 1787 CG MET 388
    ATOM 1788 SD MET 388
                                68.500 45.427 31.089 1.00 45.51
30
                                69.089 43.802 30.645 1.00 42.40
    ATOM 1789 CE MET 388
                               67.025 47.044 35.810 1.00 38.11
    ATOM 1790 C MET 388
                               67.155 48.255 35.997 1.00 38.41
    ATOM 1791 O MET 388
    ATOM 1792 N LYS 389
                               65.926 46.374 36.144 1.00 39.67
                               64.773 47.036 36.750 1.00 44.96
    ATOM 1793 CA LYS 389
35
                               63.570 46.087 36.818 1.00 49.52
    ATOM 1794 CB LYS 389
                               62.674 46.102 35.588 1.00 56.74
    ATOM 1795 CG LYS 389
    ATOM 1796 CD LYS 389
                               62.145 47.509 35.278 1.00 68.05
                               61.287 48.100 36.403 1.00 71.47
    ATOM 1797 CE LYS 389
    ATOM 1798 NZ LYS 389
                               60.038 47.330 36.661 1.00 71.98
40
                               65.041 47.604 38.141 1.00 46.60
    ATOM 1799 C LYS 389
                               64.516 48.661 38.499 1.00 47.25
    ATOM 1800 O LYS 389
    ATOM 1801 N VAL 390
                               65.832 46.893 38.935 1.00 47.15
    ATOM 1802 CA VAL 390
                               66.129 47.353 40.284 1.00 50.75
45
    ATOM 1803 CB VAL 390
                                66.686 46.202 41.182 1.00 50.42
    ATOM 1804 CG1 VAL 390
                                68.095 45.802 40.770 1.00 47.93
                                66.650 46.612 42.640 1.00 56.67
    ATOM 1805 CG2 VAL 390
                               67.072 48.558 40.286 1.00 49.82
     ATOM 1806 C VAL 390
    ATOM 1807 O VAL 390
                               66.971 49.426 41.152 1.00 52.44
                               67.926 48.651 39.272 1.00 46.14
    ATOM 1808 N GLU 391
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68.888 49.741 39.173 1.00 43.84
    ATOM 1809 CA GLU 391
                               70.150 49.268 38.449 1.00 41.44
    ATOM 1810 CB GLU 391
                               70.837 48.074 39.095 1.00 51.12
    ATOM 1811 CG GLU 391
                               71.218 48.325 40.540 1.00 57.29
    ATOM 1812 CD GLU 391
                               71.970 49.287 40.802 1.00 58.15
    ATOM 1813 OE1 GLU 391
5
    ATOM 1814 OE2 GLU 391
                               70.764 47.559 41.416 1.00 62.51
                              68.386 51.015 38.501 1.00 45.94
    ATOM 1815 C GLU 391
                              68.567 52.114 39.033 1.00 51.14
    ATOM 1816 O GLU 391
                               67.727 50.872 37.354 1.00 45.84
    ATOM 1817 N CYA 392
                              67.255 52.029 36.598 1.00 41.60
    ATOM 1818 CA CYA 392
10
    ATOM 1819 CB CYA 392
                               67.681 51.889 35.140 1.00 42.06
                               69.452 52.008 34.968 1.00 44.47
    ATOM 1820 SG CYA 392
                               69.867 50.812 33.150 1.00 54.22
    ATOM 1821 AS CYA 392
    ATOM 1822 C CYA 392
                               65.779 52.395 36.683 1.00 42.27
                               64.937 51.564 37.029 1.00 43.91
    ATOM 1823 O CYA 392
15
                              65.451 53.674 36.414 1.00 42.79
    ATOM 1824 N PRO 393
                              66.384 54.774 36.106 1.00 38.59
    ATOM 1825 CD PRO 393
                               64.067 54.159 36.459 1.00 44.20
    ATOM 1826 CA PRO 393
    ATOM 1827 CB PRO 393
                               64.218 55.667 36.238 1.00 39.88
                               65.487 55.789 35.459 1.00 35.88
    ATOM 1828 CG PRO 393
20
    ATOM 1829 C PRO 393
                              63.178 53.513 35.398 1.00 45.29
                              63.600 53.308 34.257 1.00 43.97
    ATOM 1830 O PRO 393
    ATOM 1831 N THR 394
                              61.935 53.238 35.782 1.00 48.20
                              60.959 52.607 34.901 1.00 53.71
    ATOM 1832 CA THR 394
                               59.605 52.429 35.629 1.00 59.59
25
    ATOM 1833 CB THR 394
                                58.690 51.717 34.787 1.00 66.50
    ATOM 1834 OG1 THR 394
                                59.013 53.787 36.004 1.00 61.00
    ATOM 1835 CG2 THR 394
                               60.752 53.358 33.581 1.00 51.35
     ATOM 1836 C THR 394
                               60.419 52.751 32.563 1.00 54.39
    ATOM 1837 O THR 394
                               61.008 54.664 33.595 1.00 47.65
    ATOM 1838 N GLU 395
30
                              60.845 55.509 32.414 1.00 44.43
    ATOM 1839 CA GLU 395
                               60.988 56.978 32.804 1.00 43.85
     ATOM 1840 CB GLU 395
                               61.788 55.175 31.250 1.00 42.93
     ATOM 1841 C GLU 395
     ATOM 1842 O GLU 395
                               61.589 55.649 30.129 1.00 41.39
                               62.818 54.375 31.517 1.00 39.38
    ATOM 1843 N LEU 396
35
                              63.782 53.989 30.486 1.00 35.70
     ATOM 1844 CA LEU 396
                               65.185 53.867 31.090 1.00 34.96
     ATOM 1845 CB LEU 396
                               65.854 55.141 31.609 1.00 36.47
     ATOM 1846 CG LEU 396
                               67.234 54.807 32.150 1.00 34.21
     ATOM 1847 CD1 LEU 396
                                65.959 56.164 30.491 1.00 32.74
    ATOM 1848 CD2 LEU 396
40
                               63.407 52.671 29.803 1.00 34.60
     ATOM 1849 C LEU 396
     ATOM 1850 O LEU 396
                               64.086 52.223 28.873 1.00 30.36
     ATOM 1851 N PHE 397
                               62.325 52.059 30.269 1.00 33.02
                               61.868 50.792 29.725 1.00 33.39
     ATOM 1852 CA PHE 397
                               61.615 49.782 30.852 1.00 34.30
     ATOM 1853 CB PHE 397
45
                               62.834 49.439 31.665 1.00 32.62
     ATOM 1854 CG PHE 397
                               63.296 50.301 32.654 1.00 32.35
     ATOM 1855 CD1 PHE 397
     ATOM 1856 CD2 PHE 397
                               63.504 48.241 31.461 1.00 31.28
                               64.407 49.976 33.426 1.00 27.01
     ATOM 1857 CE1 PHE 397
                               64.616 47.905 32.229 1.00 33.34
    ATOM 1858 CE2 PHE 397
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65.067 48.775 33.213 1.00 31.29
    ATOM 1859 CZ PHE 397
                              60.580 50.961 28.934 1.00 33.17
    ATOM 1860 C PHE 397
                              59.540 51.318 29.498 1.00 31.99
    ATOM 1861 O PHE 397
    ATOM 1862 N PRO 398
                              60.636 50.752 27.606 1.00 32.45
                              61.821 50.493 26.768 1.00 28.15
    ATOM 1863 CD PRO 398
5
                               59.429 50.885 26.786 1.00 30.02
    ATOM 1864 CA PRO 398
                               59.921 50.483 25.394 1.00 28.15
    ATOM 1865 CB PRO 398
                               61.352 50.923 25.397 1.00 24.89
    ATOM 1866 CG PRO 398
                              58.384 49.900 27.326 1.00 28.39
    ATOM 1867 C PRO 398
    ATOM 1868 O PRO 398
                              58.735 48.810 27.789 1.00 28.00
10
                              57.092 50.262 27.267 1.00 32.45
    ATOM 1869 N PRO 399
                               56.577 51.511 26.672 1.00 34.93
    ATOM 1870 CD PRO 399
                               55.989 49.421 27.753 1.00 32.54
    ATOM 1871 CA PRO 399
                               54.755 50.122 27.188 1.00 34.47
    ATOM 1872 CB PRO 399
                               55.159 51.564 27.196 1.00 31.37
    ATOM 1873 CG PRO 399
15
    ATOM 1874 C PRO 399
                              56.044 47.946 27.338 1.00 32.18
    ATOM 1875 O PRO 399
                               55.950 47.054 28.188 1.00 32.58
    ATOM 1876 N LEU 400
                               56.195 47.689 26.041 1.00 30.15
                              56.259 46.314 25.541 1.00 32.32
    ATOM 1877 CA LEU 400
    ATOM 1878 CB LEU 400
                               56.211 46.297 24.011 1.00 28.67
20
    ATOM 1879 CG LEU 400
                               56.028 44.927 23.351 1.00 28.77
                              54.802 44.234 23.919 1.00 22.73
    ATOM 1880 CD1 LEU 400
    ATOM 1881 CD2 LEU 400
                              55.897 45.096 21.846 1.00 27.89
                              57.496 45.561 26.051 1.00 32.27
    ATOM 1882 C LEU 400
    ATOM 1883 O LEU 400
                               57.437 44.358 26.307 1.00 32.87
25
                              58.602 46.279 26.215 1.00 32.27
    ATOM 1884 N PHE 401
    ATOM 1885 CA PHE 401
                             59.847 45.695 26.710 1.00 32.39
                              60.946 46.769 26.711 1.00 31.38
    ATOM 1886 CB PHE 401
                              62.290 46.286 27.194 1.00 35.12
    ATOM 1887 CG PHE 401
                              62.835 45.089 26.729 1.00 34.68
    ATOM 1888 CD1 PHE 401
30
    ATOM 1889 CD2 PHE 401
                                63.030 47.051 28.097 1.00 34.57
                                64.100 44.662 27.155 1.00 30.27
    ATOM 1890 CE1 PHE 401
    ATOM 1891 CE2 PHE 401
                               64.291 46.635 28.526 1.00 33.57
                               64.828 45.438 28.054 1.00 35.74
    ATOM 1892 CZ PHE 401
                              59.599 45.169 28.129 1.00 32.21
    ATOM 1893 C PHE 401
35
                               60.002 44.056 28.478 1.00 33.36
    ATOM 1894 O PHE 401
                               58.902 45.967 28.929 1.00 31.85
    ATOM 1895 N LEU 402
    ATOM 1896 CA LEU 402
                               58.582 45.602 30.302 1.00 35.06
                               57.948 46.789 31.029 1.00 34.76
    ATOM 1897 CB LEU 402
    ATOM 1898 CG LEU 402
                               58.878 47.852 31.591 1.00 33.48
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    ATOM 1899 CD1 LEU 402
                                58.060 49.010 32.152 1.00 32.58
                                59.753 47.217 32.662 1.00 26.27
    ATOM 1900 CD2 LEU 402
     ATOM 1901 C LEU 402
                               57.626 44.426 30.393 1.00 36.80
    ATOM 1902 O LEU 402
                               57.793 43.545 31.239 1.00 35.43
                               56.600 44.443 29.547 1.00 38.50
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    ATOM 1903 N GLU 403
                                55.581 43.401 29.540 1.00 40.24
     ATOM 1904 CA GLU 403
                                54.435 43.792 28.605 1.00 44.03
     ATOM 1905 CB GLU 403
                              53.239 42.850 28.666 1.00 55.53
     ATOM 1906 CG GLU 403
     ATOM 1907 CD GLU 403 52.180 43.159 27.618 1.00 66.67
    ATOM 1908 OE1 GLU 403 52.151 44.299 27.095 1.00 70.81
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51.370 42.255 27.315 1.00 73.80
    ATOM 1909 OE2 GLU 403
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    ATOM 1910 C GLU 403
                               55,745 41.029 29.805 1.00 38.78
    ATOM 1911 O GLU 403
                               56.934 41.955 28.132 1.00 37.39
    ATOM 1912 N VAL 404
                                57.475 40.686 27.652 1.00 37.05
    ATOM 1913 CA VAL 404
    ATOM 1914 CB VAL 404
                                58.180 40.855 26.286 1.00 35.57
                                 58.677 39.513 25.776 1.00 36.85
    ATOM 1915 CG1 VAL 404
                                 57.222 41.451 25.287 1.00 42.03
    ATOM 1916 CG2 VAL 404
     ATOM 1917 C VAL 404
                               58.438 40.000 28.609 1.00 38.69
                               58.436 38.774 28.727 1.00 40.71
     ATOM 1918 O VAL 404
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                               59.267 40.785 29.286 1.00 39.34
     ATOM 1919 N PHE 405
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     ATOM 1920 CA PHE 405
                                61.620 40.840 29.913 1.00 33.87
     ATOM 1921 CB PHE 405
                                62.107 40.609 28.509 1.00 32.17
     ATOM 1922 CG PHE 405
                                 62.355 41.683 27.660 1.00 31.34
     ATOM 1923 CD1 PHE 405
15
                                 62.315 39.317 28.032 1.00 31.98
     ATOM 1924 CD2 PHE 405
     ATOM 1925 CE1 PHE 405
                                62.801 41.476 26.352 1.00 30.79
                                62.759 39.099 26.730 1.00 26.06
     ATOM 1926 CE2 PHE 405
     ATOM 1927 CZ PHE 405
                                63.004 40.182 25.889 1.00 27.98
                               59.905 40.322 31.682 1.00 42.64
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     ATOM 1928 C PHE 405
                               60.785 40.188 32.534 1.00 45.10
     ATOM 1929 O PHE 405
                                58.630 40.536 31.988 1.00 48.95
     ATOM 1930 N GLU 406
                                58.181 40.641 33.373 1.00 56.93
     ATOM 1931 CA GLU 406
                                56.820 41.324 33.432 1.00 56.94
     ATOM 1932 CB GLU 406
                                58.116 39.263 34.040 1.00 61.92
     ATOM 1933 C GLU 406
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                                57.988 38.256 33.308 1.00 67.61
     ATOM 1934 O GLU 406
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              1 O1 HOH 501
     ATOM
                               68.647 41.203 12.940 1.00 39.54
     ATOM
              2 O1 HOH 502
                               64.072 40.115 12.407 1.00 32.47
              3 O1 HOH 503
     ATOM
                               62.312 39.659 16.075 1.00 17.39
              4 O1 HOH 504
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     ATOM
                               63.449 46.468 15.530 1.00 30.46
              5 O1 HOH 505
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              6 O1 HOH 506
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                               67.100 11.855 0.295 1.00 20.00
              7 O1 HOH 507
     ATOM
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              8 O1 HOH 508
     ATOM
                               59.851 10.761 6.050 1.00 20.00
              9 O1 HOH 509
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     ATOM
             10 O1 HOH 510
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     ATOM
                               54.101 13.545 8.720 1.00 20.00
             11 O1 HOH 511
     ATOM
                               55.923 15.916 12.205 1.00 29.31
             12 O1 HOH 512
     ATOM
                               50.900 19.934 8.193 1.00 20.00
             13 O1 HOH 513
     ATOM
                                50.474 22.912 7.942 1.00 45.34
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             14 O1 HOH 514
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             15 O1 HOH 515
                                50.829 25.467 13.330 1.00 20.00
             16 O1 HOH 516
     ATOM
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             17 O1 HOH 517
     ATOM
                                52.591 31.216 7.313 1.00 35.55
     ATOM
             18 O1 HOH 518
             19 O1 HOH 519
                                58.510 31.667 2.158 1.00 20.00
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                                62.484 37.992 5.537 1.00 20.00
             21 O1 HOH 521
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                                68.184 36.969 5.889 1.00 50.08
             22 O1 HOH 522
     ATOM
                                66.889 33.781 8.584 1.00 20.00
             23 O1 HOH 523
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                                67.217 30.836 3.085 1.00 34.44
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             24 O1 HOH 524
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                               76.757 22.883 5.467 1.00 36.94
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                               72.250 17.936 6.950 1.00 36.00
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             29 O1 HOH 529
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             30 O1 HOH 530
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             32 O1 HOH 532
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             33 O1 HOH 533
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                               63.169 10.413 11.722 1.00 20.00
             34 O1 HOH 534
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             37 O1 HOH 537
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                               77.187 28.903 21.137 1.00 40.22
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                               76.420 30.760 23.658 1.00 29.63
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             42 O1 HOH 542
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             43 O1 HOH 543
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     ATOM
             45 O1 HOH 545
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             52 O1 HOH 552
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             53 O1 HOH 553
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             56 O1 HOH 556
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                                75.773 46.227 30.514 1.00 29.06
             62 O1 HOH 562
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                                79.903 46.178 30.800 1.00 41.67
             63 O1 HOH 563
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             65 O1 HOH 565
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             66 O1 HOH 566
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             67 O1 HOH 567
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             68 O1 HOH 568
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             72 O1 HOH 572
                                54.188 47.024 30.900 1.00 52.93
             73 O1 HOH 573
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     ATOM
             74 O1 HOH 574
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    ATOM
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             80 O1 HOH 580
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             82 O1 HOH 582
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     END
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                               68.927 43.263 23.318 1.00 29.26
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     ATOM 2006 C3 DMT
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                               69.268 44.313 24.111 1.00 28.48
     ATOM 2007 C4 DMT
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     ATOM 2008 C5 DMT
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                               68.654 44.389 25.458 1.00 28.16
     ATOM 2009 C6 DMT
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                               68.811 42.902 20.875 1.00 26.80
     ATOM 2010 C7 DMT
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                               67.803 43.410 25.793 1.00 29.83
     ATOM 2011 C8 DMT
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     ATOM 2012 C9 DMT
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                                67.464 42.358 24.989 1.00 28.60
     ATOM 2013 C10 DMT
                                68.165 41.349 19.185 1.00 25.29
     ATOM 2014 C11 DMT
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     ATOM 2015 C12 DMT
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                                66.475 42.038 17.456 1.00 21.51
     ATOM 2016 C13 DMT
                                68.916 45.478 26.380 1.00 21.05
     ATOM 2017 C14 DMT
                                66.989 40.910 16.417 1.00 22.84
     ATOM 2018 C15 DMT
     ATOM 2019 C16 DMT
                                68.090 46.870 26.009 1.00 19.41
25
                                65.982 40.730 15.243 1.00 27.07
     ATOM 2020 C17 DMT
                                70.279 46.131 26.085 1.00 16.03
     ATOM 2021 C18 DMT
                                67.903 45.249 20.974 1.00 19.56
     ATOM 2022 C19 DMT
                                69.853 40.599 20.901 1.00 4.52
     ATOM 2023 C20 DMT
                            1
                                68.280 41.070 16.042 1.00 17.57
     ATOM 2024 N1 DMT
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                                67.209 43.465 27.087 1.00 25.94
     ATOM 2025 O1 DMT
                                69.547 43.191 22.015 1.00 30.23
     ATOM 2026 O2 DMT
                                66.449 40.778 14.118 1.00 29.45
     ATOM 2027 O3 DMT
                           1
                                64.820 40.564 15.546 1.00 26.46
     ATOM 2028 O4 DMT
35
     END
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## **APPENDIX 4**

## TR\_TRIAC.PDB

**REMARK** REMARK TR triac full length numbering REMARK Rfactor 0.236 Rfree 0.241 REMARK Resolution 25. 2.5 all reflections REMARK REMARK Three cacodylate-modified cysteines: REMARK Cys334, Cys380, Cys392 REMARK modeled as free arsenic atoms 10 REMARK REMARK conserved polar HOH numbered as in TR\_t3.pdb REMARK rearrangements start 600 REMARK REMARK side chain of certain residues modeled as ALA due to poor density; 15 REMARK however, residue name reflects true residue for clarity **REMARK** REMARK clone obtained from Murray et. al. REMARK deposited sequence confirmed, REMARK differing from that reported by Thompson et. al. 20 REMARK in the following codons: REMARK 281 Thr - Ala REMARK 285 Lys - Glu REMARK identical to that reported by Mitsuhashi et. al. REMARK gb:RNTRAVI X07409 25 M.B. MURRAY, N.D.ZILZ, AUTH JRNL N.L.MCCREARY, M.J.MACDONALD **AUTH 2 H.C.TOWLE** JRNL TITL ISOLATION AND CHARACTERIZATION OF RAT CDNA JRNL 30 **CLONES FOR TWO** TITL 2 DISTINCT THYROID HORMONE RECPTORS JRNL V. 263 25 1988 JRNL REF JBC AUTH C.C.THOMPSON, C.WEINBERGER, R.LEBO, R.M.EVANS JRNL IDENTIFICATION OF A NOVEL THYROID HORMONE TITL JRNL 35 RECEPTOR EXPRESSED TITL 2 IN THE MAMMALIAN CENTRAL NERVOUS SYSTEM JRNL V. 237 1987 **JRNL** REF SCIENCE AUTH T.MITSUHASHI, G.TENNYSON, V.NIKODEM JRNL TITL NUCLEOTIDE SEQUENCE OF NOVEL CDNAS GENERATED JRNL BY ALTERNATIVE 40 TITL 2 SPLICING OF A RAT THYROID HORMONE RECEPTOR JRNL GENE TRANSCRIPT V. 16 12 1988 REF NUC. ACIDS. RES. JRNL REMARK 9.880 -24.199 7.196 1.00 57.79 1 CB ARG 157 45 ATOM 11.380 -24.411 7.340 1.00 57.79 2 CG ARG 157 ATOM 11.960 -23.602 8.486 1.00 57.79 3 CD ARG 157 ATOM

ATOM

4 NE ARG 157

11.492 -24.098 9.778 1.00 57.79

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12.284 -24.379 10.809 1.00 57.79
             5 CZ ARG 157
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                                13.598 -24.212 10.714 1.00 57.79
    ATOM
             6 NH1 ARG 157
                                11.762 -24.854 11.932 1.00 57.79
             7 NH2 ARG 157
    ATOM
                               7.774 -24.838 5.974 1.00 38.50
    ATOM
             8 C ARG 157
                               7.553 -24.416 4.840 1.00 57.79
             9 O ARG 157
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    ATOM
             10 N ARG 157
                               9.929 -25.500 5.089 1.00 38.50
    ATOM
                                9.183 -25.276 6.360 1.00 38.50
             11 CA ARG 157
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                               6.802 -24.951 6.895 1.00 23.08
             12 N PRO 158
    ATOM
             13 CD PRO 158
                                6.945 -25.424 8.282 1.00 28.38
    ATOM
                                5.415 -24.562 6.617 1.00 23.08
             14 CA PRO 158
    ATOM
10
                                4.704 -24.824 7.948 1.00 28.38
             15 CB PRO 158
    ATOM
                                5.801 -24.735 8.966 1.00 28.38
             16 CG PRO 158
     ATOM
                               5.210 -23.124 6.132 1.00 23.08
             17 C PRO 158
     ATOM
                               5.678 -22.167 6.753 1.00 28.38
             18 O PRO 158
    ATOM
                               4.504 -23.000 5.012 1.00 19.26
             19 N GLU 159
    ATOM
15
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                                4.022 -21.912 2.878 1.00 24.58
             21 CB GLU 159
     ATOM
                                5.317 -22.009 2.086 1.00 24.58
     ATOM
             22 CG GLU 159
             23 CD GLU 159
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    ATOM
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             25 OE2 GLU 159
     ATOM
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             26 C GLU 159
     ATOM
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             27 O GLU 159
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             29 CD PRO 160
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             30 CA PRO 160
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                                1.414 -17.872 4.956 1.00 13.94
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     ATOM
                                2.880 -17.604 4.952 1.00 13.94
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             32 CG PRO 160
             33 C PRO 160
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                                0.067 -20.207 3.423 1.00 13.94
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             34 O PRO 160
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             36 CA THR 161
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             37 CB THR 161
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                                -3.441 -20.557 6.959 1.00 20.43
             38 OG1 THR 161
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             39 CG2 THR 161
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             43 CD PRO 162
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             44 CA PRO 162
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             45 CB PRO 162
             46 CG PRO 162
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                               -5.317 -18.171 3.763 1.00 12.94
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                               -5.305 -16.964 3.503 1.00 17.56
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             48 O PRO 162
                               -5.790 -18.668 4.903 1.00 19.45
             49 N GLU 163
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     ATOM
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              51 CB GLU 163
              52 CG GLU 163
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     ATOM
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              53 CD GLU 163
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     ATOM
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             56 C GLU 163
             57 O GLU 163
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             59 CA GLU 164
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     ATOM
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             62 CD GLU 164
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     ATOM
             63 OE1 GLU 164
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             64 OE2 GLU 164
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             71 CD2 TRP 165
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             72 CE2 TRP
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             73 CE3 TRP
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             75 NE1 TRP 165
     ATOM
             76 CZ2 TRP 165
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             78 CH2 TRP 165
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     ATOM
             79 C TRP 165
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                                -5.397 -12.796 4.580 1.00 14.80
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             82 CA ASP 166
     ATOM
             83 CB ASP 166
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                                -7.298 -13.999 3.403 1.00 28.74
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     ATOM
             84 CG ASP 166
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             85 OD1 ASP 166
     ATOM
             86 OD2 ASP 166
                                -8.071 -14.978 3.466 1.00 28.74
     ATOM
     ATOM
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             95 C LEU 167
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            129 CB THR 172
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            171 CB SER 177
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            172 OG SER 177
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            179 CG2 THR 178
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            184 CB ASN 179
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            202 C GLY 182
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    ATOM 218 CG TRP 185
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    ATOM 221 CE3 TRP 185
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    ATOM 231 CB LYS 186
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                               16.133 9.397 0.607 1.00 74.68
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            248 CA ARG 188
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            249 CB ARG 188
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    ATOM 257 NE ARG 189
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    ATOM 260 NH2 ARG 189
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    ATOM 266 C LYS 190
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    ATOM 273 CD2 PHE 191
    ATOM 274 CE1 PHE 191
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    ATOM 289 CA PRO 193
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            291 CG PRO 193
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            297 CG ASP 194
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            303 CA ASP 195
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    ATOM 304 CB ASP 195 22.586 23.559 20.351 1.00 85.02
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            313 CG2 ILE 196
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            398 CB LYS 209
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            410 CB ASP 211
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    ATOM 411 CG ASP 211
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    ATOM 412 OD1 ASP 211
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    ATOM 414 C ASP 211
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                               14.013 20.042 29.492 1.00 31.99
    ATOM 417 CA LEU 212
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    ATOM 420 CD1 LEU 212
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    ATOM 421 CD2 LEU 212
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            426 CB GLU 213
     ATOM
                               15.434 22.707 23.997 1.00 62.21
            427 CG GLU 213
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     ATOM 428 CD GLU 213
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     ATOM 429 OE1 GLU 213
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            454 O SER 216
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     ATOM 469 CD2 PHE 218
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     ATOM 478 OG1 THR 219
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            499 CG1 ILE 222
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    ATOM 526 CG1 ILE 226
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            557 CB VAL 230
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     ATOM 769 OE1 GLU 257
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                               14.124 1.955 12.092 1.00 26.45
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                               12.232 4.019 10.807 1.00 38.04
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    ATOM 839 NH2 ARG 266
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     ATOM 844 CB TYR 267
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     ATOM 846 CD1 TYR 267
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     ATOM 848 CD2 TYR 267
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     ATOM 849 CE2 TYR 267
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            853 O TYR 267
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    ATOM 859 OD2 ASP 268
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    ATOM 860 C ASP 268
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    ATOM 861 O ASP 268
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    ATOM 863 CD PRO 269
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    ATOM 864 CA PRO 269
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    ATOM 865 CB PRO 269
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    ATOM 866 CG PRO 269
    ATOM 867 C PRO 269
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    ATOM 868 O PRO 269
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            870 CA ALA 270
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                               25.177 5.873 7.198 1.00 41.71
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    ATOM 872 C ALA 270
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            876 CB SER 271
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    ATOM 877 OG SER 271
    ATOM
            878 C SER 271
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    ATOM 879 O SER 271
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                              24.388 6.005 14.007 1.00 41.05
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            881 CA ASP 272
    ATOM
            882 CB ASP 272
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                              25.653 5.428 16.147 1.00 47.32
            883 CG ASP 272
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    ATOM
            885 OD2 ASP 272
                              23.279 6.777 14.730 1.00 41.05
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            886 C ASP 272
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                              23.444 7.233 15.866 1.00 47.32
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            891 OG1 THR 273
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            892 CG2 THR 273
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    ATOM 894 O THR 273
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    ATOM
            897 CB LEU 274
                               16.862 6.193 16.555 1.00 22.48
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    ATOM
            898 CG LEU 274
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                               16.798 4.866 18.650 1.00 22.48
            899 CD1 LEU 274
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            902 O LEU 274
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            904 CA THR 275
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             915 CD2 LEU 276
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             917 O LEU 276
                               10.533 10.760 13.691 1.00 24.81
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            919 CA SER 277
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             921 OG SER 277
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     ATOM
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                                10.135 9.024 10.263 1.00 34.41
     ATOM
            925 CA GLY 278
     ATOM
             926 C GLY 278
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             928 N GLU 279
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             929 CA GLU 279
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            931 CG GLU 279
                                 9.202 13.631 12.014 1.00 70.24
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     ATOM
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     ATOM
             933 OE1 GLU 279
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     ATOM
            934 OE2 GLU 279
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            936 O GLU 279
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     ATOM
             938 CA MET 280
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                                13.350 14.740 17.256 1.00 33.89
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             941 SD MET 280
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            942 CE MET 280
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             944 O MET 280
                               15.797 12.690 13.080 1.00 30.24
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             946 CA ALA 281
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            948 C ALA 281
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             949 O ALA 281
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             951 CA VAL 282
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     ATOM
             952 CB VAL 282
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            953 CG1 VAL 282
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                                 16.739 10.193 18.055 1.00 37.75
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            954 CG2 VAL 282
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            956 O VAL 282
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            958 CA LYS 283
     ATOM
                                22.894 11.679 18.342 1.00 57.25
            959 CB LYS 283
     ATOM
     ATOM
            960 CG LYS 283
                                23.258 12.245 16.979 1.00 57.25
            961 CD LYS 283
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     ATOM
            962 CE LYS 283
                               24.752 13.836 15.741 1.00 57.25
     ATOM
     ATOM
            963 NZ LYS 283
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     ATOM
                               22.351 9.146 20.058 1.00 26.41
     ATOM
            966 N ARG 284
     ATOM
            967 CA ARG 284
                                22.297 8.457 21.351 1.00 26.41
                                23.527 7.566 21.528 1.00 41.02
            968 CB ARG 284
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            969 CG ARG 284
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            971 NE ARG 284
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            974 NH2 ARG 284
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            975 C ARG 284
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            976 O ARG 284
            977 N GLU 285
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            978 CA GLU 285
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                                24.366 12.258 23.492 1.00 69.82
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            979 CB GLU 285
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            980 CG GLU 285
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                                26.309 14.826 24.070 1.00 69.82
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     ATOM
            983 OE2 GLU 285
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            985 O GLU 285
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            991 OE1 GLN 286
     ATOM
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     ATOM
            993 C GLN 286
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     ATOM
            994 O GLN 286
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            995 N LEU 287
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            996 CA LEU 287
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                                15.859 8.821 22.357 1.00 21.70
     ATOM
            998 CG LEU 287
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            999 CD1 LEU 287
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     ATOM
           1000 CD2 LEU 287
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                                17.641 10.277 24.577 1.00 30.11
     ATOM 1001 C LEU 287
     ATOM 1002 O LEU 287
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     ATOM 1003 N LYS 288
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     ATOM 1004 CA LYS 288
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    ATOM 1006 CG LYS 288
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    ATOM 1007 CD LYS 288
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    ATOM 1008 CE LYS 288
                               23.866 6.568 29.224 1.00 43.14
    ATOM 1009 NZ LYS 288
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    ATOM 1010 C LYS 288
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    ATOM 1013 CA ASN 289
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    ATOM 1014 CB ASN 289
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    ATOM 1016 OD1 ASN 289
    ATOM 1017 ND2 ASN 289
                                22.566 14.253 27.149 1.00 35.61
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     ATOM 1021 CA GLY 290
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     ATOM 1025 CA GLY 291
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     ATOM 1026 C GLY 291
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     ATOM 1032 CD1 LEU 292
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     ATOM 1033 CD2 LEU 292
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     ATOM 1042 CB VAL 294
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     ATOM 1043 CG1 VAL 294
     ATOM 1044 CG2 VAL 294
                                18.315 2.887 31.697 1.00 30.11
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     ATOM 1045 C VAL 294
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                                16.056 3.118 27.698 1.00 18.14
     ATOM 1048 CA VAL 295
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     ATOM 1049 CB VAL 295
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     ATOM 1051 CG2 VAL 295
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     ATOM 1054 N SER 296
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    ATOM 1056 CB SER 296
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                               18.615 6.911 23.627 1.00 25.61
    ATOM 1057 OG SER 296
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    ATOM 1059 O SER 296
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    ATOM 1063 CG ASP 297
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    ATOM 1064 OD1 ASP 297
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    ATOM 1065 OD2 ASP 297
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    ATOM 1069 CA ALA 298
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    ATOM 1070 CB ALA 298
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     ATOM 1071 C ALA 298
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                              16.483 0.979 21.686 1.00 17.42
     ATOM 1074 CA ILE 299
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    ATOM 1075 CB ILE 299
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     ATOM 1076 CG2 ILE 299
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     ATOM 1077 CG1 ILE 299
     ATOM 1078 CD1 ILE 299
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     ATOM 1082 CA PHE 300
     ATOM 1083 CB PHE 300
                                20.804 2.854 20.409 1.00 24.01
                                20.656 4.221 19.801 1.00 24.01
     ATOM 1084 CG PHE 300
30
     ATOM 1085 CD1 PHE 300
                                19.904 5.204 20.435 1.00 24.01
     ATOM 1086 CD2 PHE 300
                                21.271 4.526 18.591 1.00 24.01
                                19.766 6.472 19.873 1.00 24.01
     ATOM 1087 CE1 PHE 300
                                21.140 5.791 18.020 1.00 24.01
     ATOM 1088 CE2 PHE 300
                               20.385 6.765 18.663 1.00 24.01
     ATOM 1089 CZ PHE 300
35
     ATOM 1090 C PHE 300
                               20.383 0.480 19.726 1.00 14.46
     ATOM 1091 O PHE 300
                               20.696 0.102 18.596 1.00 24.01
                               20.547 -0.270 20.813 1.00 21.61
     ATOM 1092 N GLU 301
                                21.123 -1.609 20.744 1.00 21.61
     ATOM 1093 CA GLU 301
     ATOM 1094 CB GLU 301
                                21.289 -2.192 22.143 1.00 23.89
40
                               20.211 -2.498 19.904 1.00 21.61
     ATOM 1095 C GLU 301
     ATOM 1096 O GLU 301
                               20.681 -3.251 19.043 1.00 23.89
     ATOM 1097 N LEU 302
                               18.906 -2.390 20.140 1.00 14.43
     ATOM 1098 CA LEU 302
                                17.922 -3.168 19.399 1.00 14.43
     ATOM 1099 CB LEU 302
                                16.512 -2.872 19.912 1.00 23.43
45
                                15.350 -3.669 19.312 1.00 23.43
     ATOM 1100 CG LEU 302
                                15.459 -5.140 19.688 1.00 23.43
     ATOM 1101 CD1 LEU 302
     ATOM 1102 CD2 LEU 302
                                14.035 -3.094 19.804 1.00 23.43
     ATOM 1103 C LEU 302
                               18.027 -2.812 17.917 1.00 14.43
                               18.089 -3.697 17.066 1.00 23.43
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     ATOM 1104 O LEU 302
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18.098 -1.515 17.625 1.00 15.17
    ATOM 1105 N GLY 303
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     ATOM 1106 CA GLY 303
    ATOM 1107 C GLY 303
                               19.411 -1.640 15.530 1.00 15.17
                               19.290 -2.137 14.406 1.00 27.67
    ATOM 1108 O GLY 303
                               20.570 -1.594 16.182 1.00 19.04
    ATOM 1109 N LYS 304
    ATOM 1110 CA LYS 304
                                21.802 -2.127 15.605 1.00 19.04
                                22.979 -1.975 16.577 1.00 56.94
    ATOM 1111 CB LYS 304
     ATOM 1112 CG LYS 304
                                23.496 -0.556 16.741 1.00 56.94
    ATOM 1113 CD LYS 304
                                24.811 -0.524 17.516 1.00 56.94
                                24.634 -0.965 18.968 1.00 56.94
    ATOM 1114 CE LYS 304
10
     ATOM 1115 NZ LYS 304
                                23.838 0.008 19.778 1.00 56.94
                               21.653 -3.596 15.229 1.00 19.04
     ATOM 1116 C LYS 304
                               21.974 -3.993 14.107 1.00 56.94
     ATOM 1117 O LYS 304
     ATOM 1118 N SER 305
                               21.146 -4.394 16.164 1.00 24.46
                                20.965 -5.822 15.932 1.00 24.46
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     ATOM 1119 CA SER 305
    ATOM 1120 CB SER 305
                                20.610 -6.533 17.240 1.00 37.46
     ATOM 1121 OG SER 305
                                19.444 -5.984 17.827 1.00 37.46
                               19.926 -6.128 14.853 1.00 24.46
     ATOM 1122 C SER 305
                               20.146 -6.996 14.006 1.00 37.46
     ATOM 1123 O SER 305
                               18.819 -5.390 14.858 1.00 25.47
     ATOM 1124 N LEU 306
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                                17.753 -5.592 13.881 1.00 25.47
     ATOM 1125 CA LEU 306
                                16.525 -4.746 14.224 1.00 15.99
     ATOM 1126 CB LEU 306
                                15.700 -5.190 15.432 1.00 15.99
     ATOM 1127 CG LEU 306
                                 14.504 -4.271 15.600 1.00 15.99
     ATOM 1128 CD1 LEU 306
                                 15.244 -6.624 15.247 1.00 15.99
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     ATOM 1129 CD2 LEU 306
     ATOM 1130 C LEU 306
                               18.174 -5.330 12.439 1.00 25.47
                               17.596 -5.902 11.513 1.00 15.99
     ATOM 1131 O LEU 306
                               19.182 -4.482 12.247 1.00 24.28
     ATOM 1132 N SER 307
     ATOM 1133 CA SER 307
                                19.670 -4.160 10.907 1.00 24.28
                                20.910 -3.263 10.989 1.00 40.92
     ATOM 1134 CB SER 307
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     ATOM 1135 OG SER 307
                                20.617 -2.028 11.622 1.00 40.92
     ATOM 1136 C SER 307
                               19.995 -5.422 10.107 1.00 24.28
     ATOM 1137 O SER 307
                               19.625 -5.535 8.936 1.00 40.92
                                20.644 -6.383 10.761 1.00 30.97
     ATOM 1138 N ALA 308
                                21.027 -7.640 10.124 1.00 30.97
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     ATOM 1139 CA ALA 308
     ATOM 1140 CB ALA 308
                                22.004 -8.399 11.013 1.00 37.84
                                19.830 -8.528 9.779 1.00 30.97
     ATOM 1141 C ALA 308
                                19.897 -9.336 8.853 1.00 37.84
     ATOM 1142 O ALA 308
     ATOM 1143 N PHE 309
                               18.737 -8.372 10.520 1.00 22.78
                                17.533 -9.166 10.292 1.00 22.78
     ATOM 1144 CA PHE 309
40
     ATOM 1145 CB PHE 309
                                16.571 -9.037 11.477 1.00 30.14
     ATOM 1146 CG PHE 309
                                17.032 -9.751 12.716 1.00 30.14
                                 16.299 -10.809 13.236 1.00 30.14
     ATOM 1147 CD1 PHE 309
                                 18.204 -9.372 13.359 1.00 30.14
     ATOM 1148 CD2 PHE 309
     ATOM 1149 CE1 PHE 309
                                 16.725 -11.481 14.378 1.00 30.14
45
                                 18.640 -10.038 14.503 1.00 30.14
     ATOM 1150 CE2 PHE 309
                                17.896 -11.094 15.013 1.00 30.14
     ATOM 1151 CZ PHE 309
     ATOM 1152 C PHE 309
                               16.818 -8.813 8.990 1.00 22.78
                               16.068 -9.631 8.451 1.00 30.14
     ATOM 1153 O PHE 309
                               17.051 -7.598 8.496 1.00 35.30
     ATOM 1154 N ASN 310
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16.441 -7.109 7.255 1.00 35.30
     ATOM 1155 CA ASN 310
                                17.109 -7.760 6.037 1.00 28.28
     ATOM 1156 CB ASN 310
                               14.929 -7.339 7.229 1.00 35.30
     ATOM 1157 C ASN 310
     ATOM 1158 O ASN 310
                               14.395 -7.970 6.312 1.00 28.28
                               14.249 -6.831 8.251 1.00 27.52
     ATOM 1159 N LEU 311
 5
                              12.803 -6.979 8.369 1.00 27.52
     ATOM 1160 CA LEU 311
                               12.351 -6.630 9.788 1.00 22.62
     ATOM 1161 CB LEU 311
                               12.950 -7.396 10.968 1.00 22.62
     ATOM 1162 CG LEU 311
                                12.360 -6.864 12.268 1.00 22.62
     ATOM 1163 CD1 LEU 311
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     ATOM 1164 CD2 LEU 311
                                12.672 -8.881 10.821 1.00 22.62
                               12.060 -6.085 7.382 1.00 27.52
     ATOM 1165 C LEU 311
                               12.519 -4.986 7.067 1.00 22.62
     ATOM 1166 O LEU 311
                               10.918 -6.563 6.892 1.00 16.74
     ATOM 1167 N ASP 312
                               10.095 -5.789 5.968 1.00 16.74
     ATOM 1168 CA ASP 312
                                9.803 -6.578 4.673 1.00 16.35
     ATOM 1169 CB ASP 312
15
                                8.924 -7.814 4.888 1.00 16.35
     ATOM 1170 CG ASP 312
                                8.591 -8.168 6.037 1.00 16.35
     ATOM 1171 OD1 ASP 312
     ATOM 1172 OD2 ASP 312
                                 8.559 -8.446 3.876 1.00 16.35
                               8.808 -5.354 6.678 1.00 16.74
     ATOM 1173 C ASP 312
     ATOM 1174 O ASP 312
                               8.535 -5.798 7.797 1.00 16.35
20
                               8.007 -4.520 6.019 1.00 5.43
     ATOM 1175 N ASP 313
                                6.758 -4.016 6.592 1.00 5.43
     ATOM 1176 CA ASP 313
                                5.974 -3.201 5.559 1.00 31.80
     ATOM 1177 CB ASP 313
                                6.670 -1.906 5.183 1.00 31.80
     ATOM 1178 CG ASP 313
                                7.392 -1.340 6.033 1.00 31.80
     ATOM 1179 OD1 ASP 313
25
     ATOM 1180 OD2 ASP 313
                                 6.493 -1.452 4.032 1.00 31.80
                               5.849 -5.081 7.189 1.00 5.43
     ATOM 1181 C ASP 313
                               5.216 -4.849 8.221 1.00 31.80
     ATOM 1182 O ASP 313
                               5.777 -6.238 6.543 1.00 12.98
     ATOM 1183 N THR 314
30
     ATOM 1184 CA THR 314
                                4.934 -7.327 7.022 1.00 12.98
                                4.825 -8.441 5.968 1.00 18.90
     ATOM 1185 CB THR 314
                                 4.249 -7.904 4.769 1.00 18.90
     ATOM 1186 OG1 THR 314
     ATOM 1187 CG2 THR 314
                                 3.960 -9.578 6.477 1.00 18.90
                               5.426 -7.910 8.349 1.00 12.98
     ATOM 1188 C THR 314
                               4.636 -8.124 9.268 1.00 18.90
     ATOM 1189 O THR 314
35
                                6.731 -8.135 8.457 1.00 9.13
     ATOM 1190 N GLU 315
                                7.316 -8.685 9.675 1.00 9.13
     ATOM 1191 CA GLU 315
     ATOM 1192 CB GLU 315
                                8.771 -9.078 9.427 1.00 11.49
                                 8.870 -10.323 8.562 1.00 11.49
     ATOM 1193 CG GLU 315
     ATOM 1194 CD GLU 315
                                10.233 -10.544 7.945 1.00 11.49
40
                                10.964 -9.561 7.705 1.00 11.49
     ATOM 1195 OE1 GLU 315
                                10.558 -11.715 7.669 1.00 11.49
     ATOM 1196 OE2 GLU 315
     ATOM 1197 C GLU 315
                                7.180 -7.720 10.847 1.00 9.13
                                6.863 -8.131 11.967 1.00 11.49
     ATOM 1198 O GLU 315
     ATOM 1199 N VAL 316
45
                                7.376 -6.433 10.575 1.00 9.46
     ATOM 1200 CA VAL 316
                                7.240 -5.406 11.602 1.00 9.46
                                7.655 -4.015 11.063 1.00 7.95
     ATOM 1201 CB VAL 316
                                 7,434 -2.941 12.124 1.00 7.95
     ATOM 1202 CG1 VAL 316
     ATOM 1203 CG2 VAL 316
                                 9.112 -4.037 10.625 1.00 7.95
                                5.777 -5.365 12.051 1.00 9.46
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     ATOM 1204 C VAL 316
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ATOM 1205 O VAL 316
                                5.484 -5.300 13.247 1.00 7.95
    ATOM 1206 N ALA 317
                                4.866 -5.438 11.083 1.00 5.52
    ATOM 1207 CA ALA 317
                                3.434 -5.417 11.355 1.00 5.52
                                2.656 -5.415 10.054 1.00 10.98
    ATOM 1208 CB ALA 317
     ATOM 1209 C ALA 317
                                3.002 -6.595 12.225 1.00 5.52
    ATOM 1210 O ALA 317
                                2.317 -6.412 13.230 1.00 10.98
                                3.411 -7.799 11.838 1.00 8.62
    ATOM 1211 N LEU 318
                                3.067 -9.003 12.584 1.00 8.62
    ATOM 1212 CA LEU 318
    ATOM 1213 CB LEU 318
                                3.523 -10.249 11.825 1.00 10.49
     ATOM 1214 CG LEU 318
                                2.770 -10.494 10.514 1.00 10.49
10
     ATOM 1215 CD1 LEU 318
                                 3.376 -11.664 9.769 1.00 10.49
    ATOM 1216 CD2 LEU 318
                                 1.297 -10.741 10.799 1.00 10.49
                                3.674 -8.971 13.978 1.00 8.62
     ATOM 1217 C LEU 318
                                3.047 -9.407 14.945 1.00 10.49
     ATOM 1218 O LEU 318
                                4.885 -8.435 14.082 1.00 9.43
     ATOM 1219 N LEU 319
15
                                5.560 -8.325 15.366 1.00 9.43
     ATOM 1220 CA LEU 319
     ATOM 1221 CB LEU 319
                                6.975 -7.773 15.173 1.00 24.05
                                7.901 -7.680 16.389 1.00 24.05
     ATOM 1222 CG LEU 319
                                 7.889 -8.977 17.182 1.00 24.05
     ATOM 1223 CD1 LEU 319
     ATOM 1224 CD2 LEU 319
                                 9.310 -7.356 15.922 1.00 24.05
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     ATOM 1225 C LEU 319
                                4.731 -7.404 16.259 1.00 9.43
     ATOM 1226 O LEU 319
                                4.456 -7.731 17.416 1.00 24.05
     ATOM 1227 N GLN 320
                                4.287 -6.282 15.699 1.00 8.67
                                 3,467 -5.325 16.437 1.00 8.67
     ATOM 1228 CA GLN 320
25
     ATOM 1229 CB GLN 320
                                 3.151 -4.102 15.573 1.00 10.94
     ATOM 1230 CG GLN 320
                                 4.361 -3.256 15.218 1.00 10.94
                                 4.025 -2.045 14.359 1.00 10.94
     ATOM 1231 CD GLN 320
     ATOM 1232 OE1 GLN 320
                                 4.889 -1.217 14.082 1.00 10.94
     ATOM 1233 NE2 GLN 320
                                 2.773 -1.940 13.924 1.00 10.94
                                2.169 -5.984 16.895 1.00 8.67
     ATOM 1234 C GLN 320
30
     ATOM 1235 O GLN 320
                                1.708 -5.751 18.013 1.00 10.94
     ATOM 1236 N ALA 321
                                1.586 -6.806 16.028 1.00 9.21
     ATOM 1237 CA ALA 321
                                 0.349 -7.513 16.342 1.00 9.21
                                -0.136 -8.283 15.129 1.00 12.83
     ATOM 1238 CB ALA 321
     ATOM 1239 C ALA 321
                                0.558 -8.460 17.523 1.00 9.21
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     ATOM 1240 O ALA 321
                               -0.315 -8.591 18.382 1.00 12.83
     ATOM 1241 N VAL 322
                                1.718 -9.111 17.566 1.00 9.10
                                 2.043 -10.030 18.651 1.00 9.10
     ATOM 1242 CA VAL 322
     ATOM 1243 CB VAL 322
                                 3.340 -10.827 18.352 1.00 15.92
                                 3.783 -11.614 19.575 1.00 15.92
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     ATOM 1244 CG1 VAL 322
                                 3.106 -11.780 17.194 1.00 15.92
     ATOM 1245 CG2 VAL 322
     ATOM 1246 C VAL 322
                                2.192 -9.256 19.960 1.00 9.10
                                1.707 -9.691 21.003 1.00 15.92
     ATOM 1247 O VAL 322
     ATOM 1248 N LEU 323
                                2.856 -8.106 19.893 1.00 11.07
     ATOM 1249 CA LEU 323
                                 3.062 -7.257 21.064 1.00 11.07
45
                                3.959 -6.070 20.705 1.00 16.31
     ATOM 1250 CB LEU 323
     ATOM 1251 CG LEU 323
                                 5,377 -6,393 20,229 1,00 16,31
     ATOM 1252 CD1 LEU 323
                                 6.039 -5.149 19.669 1.00 16.31
     ATOM 1253 CD2 LEU 323
                                 6.187 -6.966 21.375 1.00 16.31
     ATOM 1254 C LEU 323
                                1.729 -6.742 21.595 1.00 11.07
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1.523 -6.650 22.803 1.00 16.31
     ATOM 1255 O LEU 323
     ATOM 1256 N LEU 324
                                0.827 -6.413 20.677 1.00 13.48
                                -0.494 -5.900 21.015 1.00 13.48
     ATOM 1257 CA LEU 324
                                -1.185 -5.383 19.752 1.00 15.92
     ATOM 1258 CB LEU 324
     ATOM 1259 CG LEU 324
                                -2.607 -4.837 19.889 1.00 15.92
     ATOM 1260 CD1 LEU 324
                                 -2.602 -3.547 20.692 1.00 15.92
                                 -3.182 -4.598 18.511 1.00 15.92
     ATOM 1261 CD2 LEU 324
                               -1.393 -6.924 21.707 1.00 13.48
     ATOM 1262 C LEU 324
     ATOM 1263 O LEU 324
                                -1.896 -6.678 22.802 1.00 15.92
                                -1.593 -8.074 21.072 1.00 11.47
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     ATOM 1264 N MET 325
                                 -2.458 -9.111 21.631 1.00 11.47
     ATOM 1265 CA MET 325
                                 -2.959 -10.043 20.520 1.00 22.90
     ATOM 1266 CB MET 325
     ATOM 1267 CG MET 325
                                -3.689 -9.347 19.375 1.00 22.90
                                -5.052 -8.287 19.908 1.00 22.90
     ATOM 1268 SD MET 325
     ATOM 1269 CE MET 325
                                -6.284 -9.475 20.353 1.00 22.90
15
     ATOM 1270 C MET 325
                                -1.814 -9.932 22.752 1.00 11.47
     ATOM 1271 O MET 325
                                -1.899 -11.160 22.758 1.00 22.90
                               -1.193 -9.256 23.711 1.00 30.07
     ATOM 1272 N SER 326
     ATOM 1273 CA SER 326
                                -0.543 -9.936 24.826 1.00 30.07
                                0.723 -9.175 25.239 1.00 32.79
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     ATOM 1274 CB SER 326
     ATOM 1275 OG SER 326
                                1.283 -9.699 26.433 1.00 32.79
                               -1.492 -10.061 26.014 1.00 30.07
     ATOM 1276 C SER 326
     ATOM 1277 O SER 326
                               -2.343 -9.198 26.235 1.00 32.79
                                -1.347 -11.143 26.773 1.00 29.08
     ATOM 1278 N THR 327
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     ATOM 1279 CA THR 327
                                -2.179 -11.368 27.948 1.00 29.08
     ATOM 1280 CB THR 327
                                -2.705 -12.817 27.998 1.00 36.96
     ATOM 1281 OG1 THR 327
                                 -1.612 -13.734 27.856 1.00 36.96
     ATOM 1282 CG2 THR 327
                                 -3.716 -13.055 26.890 1.00 36.96
     ATOM 1283 C THR 327
                                -1.426 -11.049 29.239 1.00 29.08
                                -1.930 -11.295 30.333 1.00 36.96
     ATOM 1284 O THR 327
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     ATOM 1285 N ASP 328
                               -0.214 -10.513 29.111 1.00 38.93
     ATOM 1286 CA ASP 328
                                 0.596 -10.152 30.273 1.00 38.93
     ATOM 1287 CB ASP 328
                                2.082 -10.089 29.899 1.00 85.70
                                 2.660 -11.451 29.556 1.00 85.70
     ATOM 1288 CG ASP 328
                                 3.388 -11.554 28.542 1.00 85.70
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     ATOM 1289 OD1 ASP 328
     ATOM 1290 OD2 ASP 328
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     ATOM 1291 C ASP 328
                                0.148 -8.810 30.845 1.00 38.93
     ATOM 1292 O ASP 328
                                0.962 -7.911 31.061 1.00 85.70
     ATOM 1293 N ARG 329
                                -1.154 -8.673 31.070 1.00 28.95
     ATOM 1294 CA ARG 329
                                 -1.716 -7.445 31.608 1.00 28.95
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                                 -2.390 -6.612 30.509 1.00 38.88
     ATOM 1295 CB ARG 329
                                 -1.449 -5.887 29.554 1.00 38.88
     ATOM 1296 CG ARG 329
     ATOM 1297 CD ARG 329
                                 -1.107 -6.739 28.347 1.00 38.88
     ATOM 1298 NE ARG 329
                                 -0.322 -6.005 27.356 1.00 38.88
                                 1.006 -5.936 27.351 1.00 38.88
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     ATOM 1299 CZ ARG 329
                                  1.713 -6.552 28.290 1.00 38.88
     ATOM 1300 NH1 ARG 329
     ATOM 1301 NH2 ARG 329
                                  1.631 -5.270 26.391 1.00 38.88
     ATOM 1302 C ARG 329
                                -2.745 -7.790 32.672 1.00 28.95
     ATOM 1303 O ARG 329
                                -3.279 -8.898 32.696 1.00 38.88
     ATOM 1304 N SER 330
                               -3.029 -6.829 33.542 1.00 42.07
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-3.999 -7.025 34.607 1.00 42.07
     ATOM 1305 CA SER 330
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     ATOM 1306 CB SER 330
                               -5.340 -6.413 34.220 1.00 42.07
     ATOM 1307 C SER 330
                               -5.386 -5.382 33.550 1.00 37.35
     ATOM 1308 O SER 330
                                -6.424 -7.085 34.598 1.00 26.57
     ATOM 1309 N GLY 331
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                                 -7.754 -6.572 34.318 1.00 26.57
     ATOM 1310 CA GLY 331
                                -8.404 -6.915 32.991 1.00 26.57
     ATOM 1311 C GLY 331
                                -9.462 -6.371 32.671 1.00 30.06
     ATOM 1312 O GLY 331
                                -7.797 -7.807 32.214 1.00 31.47
     ATOM 1313 N LEU 332
     ATOM 1314 CA LEU 332
                                -8.374 -8.189 30.928 1.00 31.47
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     ATOM 1315 CB LEU 332
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                                 -6.261 -8.076 29.425 1.00 23.83
     ATOM 1316 CG LEU 332
                                 -5.296 -8.960 28.652 1.00 23.83
     ATOM 1317 CD1 LEU 332
     ATOM 1318 CD2 LEU 332
                                 -6.897 -7.041 28.509 1.00 23.83
     ATOM 1319 C LEU 332
                                -9.630 -9.039 31.091 1.00 31.47
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     ATOM 1320 O LEU 332
                                -9.665 -9.969 31.895 1.00 23.83
                               -10.659 -8.702 30.321 1.00 27.66
     ATOM 1321 N LEU 333
     ATOM 1322 CA LEU 333
                                -11.927 -9.422 30.351 1.00 27.66
     ATOM 1323 CB LEU 333
                                -13.072 -8.500 29.918 1.00 49.79
                                -13.416 -7.312 30.820 1.00 49.79
     ATOM 1324 CG LEU 333
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                                -14.328 -6.339 30.083 1.00 49.79
     ATOM 1325 CD1 LEU 333
     ATOM 1326 CD2 LEU 333
                                -14.072 -7.803 32.104 1.00 49.79
                               -11.904 -10.663 29.456 1.00 27.66
     ATOM 1327 C LEU 333
                               -12.117 -11.780 29.919 1.00 49.79
     ATOM 1328 O LEU 333
                               -11.616 -10.464 28.174 1.00 29.56
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     ATOM 1329 N CYS 334
                                -11.583 -11.566 27.220 1.00 29.56
     ATOM 1330 CA CYS 334
     ATOM 1331 CB CYS 334
                                -12.134 -11.106 25.865 1.00 47.01
                                -13.888 -10.657 25.883 1.00 47.01
     ATOM 1332 SG CYS 334
                               -10.187 -12.161 27.050 1.00 29.56
     ATOM 1333 C CYS 334
                                -9.652 -12.202 25.942 1.00 47.01
     ATOM 1334 O CYS 334
30
                                -9.617 -12.655 28.147 1.00 30.69
     ATOM 1335 N VAL 335
                                 -8.280 -13.250 28.132 1.00 30.69
     ATOM 1336 CA VAL 335
                                 -7.913 -13.844 29.514 1.00 32.18
     ATOM 1337 CB VAL 335
     ATOM 1338 CG1 VAL 335
                                 -6.517 -14.456 29.480 1.00 32.18
     ATOM 1339 CG2 VAL 335
                                 -7.988 -12.768 30.584 1.00 32.18
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                                -8.120 -14.340 27.068 1.00 30.69
     ATOM 1340 C VAL 335
     ATOM 1341 O VAL 335
                                -7.149 -14.337 26.309 1.00 32.18
                                -9.079 -15.260 27.012 1.00 30.13
     ATOM 1342 N ASP 336
     ATOM 1343 CA ASP 336
                                -9.040 -16.360 26.052 1.00 30.13
                                -10.218 -17.311 26.284 1.00 63.22
     ATOM 1344 CB ASP 336
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     ATOM 1345 CG ASP 336
                                -10.178 -18.528 25.370 1.00 63.22
     ATOM 1346 OD1 ASP 336
                                -11.119 -18.700 24.565 1.00 63.22
                                 -9.205 -19.311 25.452 1.00 63.22
     ATOM 1347 OD2 ASP 336
                                -9.012 -15.903 24.594 1.00 30.13
     ATOM 1348 C ASP 336
                                -8.156 -16.339 23.823 1.00 63.22
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     ATOM 1349 O ASP 336
                                -9.944 -15.027 24.223 1.00 26.63
     ATOM 1350 N LYS 337
                                -10.024 -14.515 22.856 1.00 26.63
     ATOM 1351 CA LYS 337
     ATOM 1352 CB LYS 337
                                -11.172 -13.516 22.729 1.00 21.38
                                -8.706 -13.865 22.438 1.00 26.63
     ATOM 1353 C LYS 337
                                -8.204 -14.110 21.338 1.00 21.38
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     ATOM 1354 O LYS 337
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ATOM 1355 N ILE 338
                               -8.141 -13.060 23.334 1.00 24.65
                                -6.879 -12.376 23.078 1.00 24.65
     ATOM 1356 CA ILE 338
                                -6.543 -11.380 24.215 1.00 20.45
    ATOM 1357 CB ILE 338
                                -5.198 -10.719 23.966 1.00 20.45
    ATOM 1358 CG2 ILE 338
                                -7.632 -10.308 24.308 1.00 20.45
     ATOM 1359 CG1 ILE 338
     ATOM 1360 CD1 ILE 338
                                -7.479 -9.374 25.486 1.00 20.45
                               -5.744 -13.388 22.911 1.00 24.65
     ATOM 1361 C ILE 338
                               -4.948 -13.288 21.974 1.00 20.45
     ATOM 1362 O ILE 338
                                -5.700 -14.383 23.795 1.00 35.34
     ATOM 1363 N GLU 339
                                 -4.673 -15.422 23.745 1.00 35.34
     ATOM 1364 CA GLU 339
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                                 -4.836 -16.388 24.916 1.00 29.51
     ATOM 1365 CB GLU 339
     ATOM 1366 C GLU 339
                                -4.744 -16.180 22.421 1.00 35.34
     ATOM 1367 O GLU 339
                                -3.720 -16.421 21.777 1.00 29.51
     ATOM 1368 N LYS 340
                                -5.959 -16.536 22.009 1.00 24.19
                                -6.168 -17.256 20.755 1.00 24.19
     ATOM 1369 CA LYS 340
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     ATOM 1370 CB LYS 340
                                -7.627 -17.671 20.624 1.00 23.97
     ATOM 1371 C LYS 340
                                -5.754 -16.377 19.576 1.00 24.19
                                -5.197 -16.860 18.586 1.00 23.97
     ATOM 1372 O LYS 340
     ATOM 1373 N SER 341
                                -6.000 -15.079 19.708 1.00 16.85
                                -5.651 -14.115 18.676 1.00 16.85
     ATOM 1374 CA SER 341
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     ATOM 1375 CB SER 341
                                -6.223 -12.744 19.033 1.00 26.59
     ATOM 1376 OG SER 341
                                -5.852 -11.765 18.080 1.00 26.59
     ATOM 1377 C SER 341
                                -4.137 -14.026 18.500 1.00 16.85
                                -3.638 -14.042 17.374 1.00 26.59
     ATOM 1378 O SER 341
                                -3.406 -13.932 19.608 1.00 17.35
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     ATOM 1379 N GLN 342
     ATOM 1380 CA GLN 342
                                 -1.952 -13.845 19.537 1.00 17.35
                                 -1.337 -13.597 20.913 1.00 30.07
     ATOM 1381 CB GLN 342
                                 0.140 -13.245 20.832 1.00 30.07
     ATOM 1382 CG GLN 342
                                 0.811 -13.196 22.182 1.00 30.07
     ATOM 1383 CD GLN 342
                                  0.884 -14.201 22.884 1.00 30.07
     ATOM 1384 OE1 GLN 342
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                                  1.318 -12.030 22.548 1.00 30.07
     ATOM 1385 NE2 GLN 342
     ATOM 1386 C GLN 342
                                -1.368 -15.118 18.944 1.00 17.35
     ATOM 1387 O GLN 342
                                -0.405 -15.066 18.178 1.00 30.07
     ATOM 1388 N GLU 343
                                -1.949 -16.260 19.303 1.00 18.35
                                 -1.489 -17.546 18.791 1.00 18.35
     ATOM 1389 CA GLU 343
35
                                 -2.308 -18.676 19.394 1.00 16.98
     ATOM 1390 CB GLU 343
                                -1.603 -17.560 17.267 1.00 18.35
     ATOM 1391 C GLU 343
                                -0.699 -18.026 16.568 1.00 16.98
     ATOM 1392 O GLU 343
     ATOM 1393 N ALA 344
                                -2.706 -17.017 16.761 1.00 14.83
                                 -2.946 -16.948 15.324 1.00 14.83
     ATOM 1394 CA ALA 344
40
                                 -4.327 -16.376 15.049 1.00 19.42
     ATOM 1395 CB ALA 344
     ATOM 1396 C ALA 344
                                -1.872 -16.102 14.640 1.00 14.83
                                -1.311 -16.507 13.619 1.00 19.42
     ATOM 1397 O ALA 344
                                -1.586 -14.934 15.211 1.00 13.10
     ATOM 1398 N TYR 345
     ATOM 1399 CA TYR 345
                                 -0.569 -14.041 14.665 1.00 13.10
45
                                 -0.573 -12.697 15.393 1.00 2.00
     ATOM 1400 CB TYR 345
                                 -1.670 -11.767 14.938 1.00 2.00
     ATOM 1401 CG TYR 345
     ATOM 1402 CD1 TYR 345
                                 -2.707 -11.409 15.794 1.00 2.00
                                 -3.722 -10.562 15.377 1.00 2.00
     ATOM 1403 CE1 TYR 345
                                 -1.674 -11.248 13.647 1.00 2.00
     ATOM 1404 CD2 TYR 345
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-2.683 -10.398 13.219 1.00 2.00
     ATOM 1405 CE2 TYR 345
     ATOM 1406 CZ TYR 345
                                -3.706 -10.061 14.087 1.00 2.00
                                 -4.722 -9.233 13.669 1.00 2.00
     ATOM 1407 OH TYR 345
                                0.818 -14.666 14.732 1.00 13.10
     ATOM 1408 C TYR 345
     ATOM 1409 O TYR 345
                                1.614 -14.504 13.811 1.00 2.00
 5
                                1.101 -15.387 15.813 1.00 12.59
     ATOM 1410 N LEU 346
     ATOM 1411 CA LEU 346
                                 2.396 -16.041 15.976 1.00 12.59
                                 2.498 -16.715 17.347 1.00 22.61
     ATOM 1412 CB LEU 346
                                 2.899 -15.799 18.504 1.00 22.61
     ATOM 1413 CG LEU 346
     ATOM 1414 CD1 LEU 346
                                 2.717 -16.511 19.830 1.00 22.61
10
                                 4.341 -15.357 18.324 1.00 22.61
     ATOM 1415 CD2 LEU 346
                                2.629 -17.057 14.865 1.00 12.59
     ATOM 1416 C LEU 346
                                3.706 -17.099 14.272 1.00 22.61
     ATOM 1417 O LEU 346
     ATOM 1418 N LEU 347
                                1.612 -17.862 14.574 1.00 18.42
                                 1.706 -18.863 13.517 1.00 18.42
     ATOM 1419 CA LEU 347
15
                                 0.471 -19.762 13.512 1.00 23.56
     ATOM 1420 CB LEU 347
                                 0.509 -20.965 14.456 1.00 23.56
     ATOM 1421 CG LEU 347
     ATOM 1422 CD1 LEU 347
                                 -0.819 -21.702 14.398 1.00 23.56
                                 1.659 -21.890 14.068 1.00 23.56
     ATOM 1423 CD2 LEU 347
     ATOM 1424 C LEU 347
                                1.870 -18.201 12.154 1.00 18.42
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                                2.672 -18.651 11.330 1.00 23.56
     ATOM 1425 O LEU 347
                                1.099 -17.144 11.917 1.00 12.49
     ATOM 1426 N ALA 348
                                 1.157 -16.403 10.663 1.00 12.49
     ATOM 1427 CA ALA 348
                                 0.098 -15.302 10.654 1.00 14.77
     ATOM 1428 CB ALA 348
                                2.545 -15.798 10.504 1.00 12.49
     ATOM 1429 C ALA 348
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                                3.154 - 15.874 9.436 1.00 14.77
     ATOM 1430 O ALA 348
                                3.048 -15.246 11.602 1.00 15.52
     ATOM 1431 N PHE 349
                                 4.357 -14.613 11.664 1.00 15.52
     ATOM 1432 CA PHE 349
                                 4.566 -14.049 13.076 1.00 14.41
     ATOM 1433 CB PHE 349
     ATOM 1434 CG PHE 349
                                 5.714 -13.085 13.203 1.00 14.41
30
                                 6.473 -12.712 12.099 1.00 14.41
     ATOM 1435 CD1 PHE 349
                                 6.027 -12.540 14.443 1.00 14.41
     ATOM 1436 CD2 PHE 349
     ATOM 1437 CE1 PHE 349
                                 7.523 -11.813 12.230 1.00 14.41
                                 7.075 -11.640 14.584 1.00 14.41
     ATOM 1438 CE2 PHE 349
                                 7.825 -11.275 13.475 1.00 14.41
     ATOM 1439 CZ PHE 349
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                                5.444 -15.633 11.324 1.00 15.52
     ATOM 1440 C PHE 349
     ATOM 1441 O PHE 349
                                6.252 -15.413 10.422 1.00 14.41
     ATOM 1442 N GLU 350
                                5.439 -16.760 12.026 1.00 13.20
                                 6.424 -17.811 11.801 1.00 13.20
     ATOM 1443 CA GLU 350
     ATOM 1444 CB GLU 350
                                 6.152 -18.995 12.734 1.00 33.43
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                                 7.068 -20.193 12.519 1.00 33.43
     ATOM 1445 CG GLU 350
                                 6.786 -21.331 13.482 1.00 33.43
     ATOM 1446 CD GLU 350
                                  7.746 -22.035 13.857 1.00 33.43
     ATOM 1447 OE1 GLU 350
                                  5.611 -21.525 13.865 1.00 33.43
     ATOM 1448 OE2 GLU 350
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     ATOM 1449 C GLU 350
                                6.409 -18.283 10.352 1.00 13.20
                                7.449 -18.355 9.694 1.00 33.43
     ATOM 1450 O GLU 350
                                5.217 -18.573 9.850 1.00 19.10
     ATOM 1451 N HIS 351
                                5.062 -19.051 8.485 1.00 19.10
     ATOM 1452 CA HIS 351
                                3.632 -19.536 8.256 1.00 18.97
     ATOM 1453 CB HIS 351
                                3.249 -20.700 9.117 1.00 18.97
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     ATOM 1454 CG HIS 351
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3.987 -21.474 9.948 1.00 18.97
    ATOM 1455 CD2 HIS 351
                                1.960 -21.180 9.194 1.00 18.97
     ATOM 1456 ND1 HIS 351
    ATOM 1457 CE1 HIS 351
                                1.918 -22.195 10.039 1.00 18.97
                                3.134 -22.394 10.509 1.00 18.97
    ATOM 1458 NE2 HIS 351
                               5.477 -18.011 7.449 1.00 19.10
     ATOM 1459 C HIS 351
    ATOM 1460 O HIS 351
                               5.955 -18.366 6.371 1.00 18.97
                                5.304 -16.732 7.767 1.00 9.38
    ATOM 1461 N TYR 352
                                 5.711 -15.683 6.843 1.00 9.38
     ATOM 1462 CA TYR 352
     ATOM 1463 CB TYR 352
                                 5.168 -14.317 7.257 1.00 16.06
                                 5.539 -13.238 6.268 1.00 16.06
     ATOM 1464 CG TYR 352
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                                 4.939 -13.190 5.008 1.00 16.06
     ATOM 1465 CD1 TYR 352
                                 5.321 -12.242 4.060 1.00 16.06
     ATOM 1466 CE1 TYR 352
                                 6.531 -12.303 6.562 1.00 16.06
     ATOM 1467 CD2 TYR 352
                                 6.923 -11.349 5.620 1.00 16.06
     ATOM 1468 CE2 TYR 352
                                6.313 -11.326 4.371 1.00 16.06
    ATOM 1469 CZ TYR 352
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                                 6.710 -10.401 3.431 1.00 16.06
     ATOM 1470 OH TYR 352
                                7.234 -15.639 6.812 1.00 9.38
     ATOM 1471 C TYR 352
                                7.838 -15.475   5.751   1.00   16.06
     ATOM 1472 O TYR 352
                                7.851 -15.789 7.980 1.00 15.38
     ATOM 1473 N VAL 353
                                 9.305 -15.790 8.087 1.00 15.38
     ATOM 1474 CA VAL 353
20
                                 9.761 -15.945 9.558 1.00 18.40
     ATOM 1475 CB VAL 353
                                 11.262 -16.163 9.633 1.00 18.40
     ATOM 1476 CG1 VAL 353
     ATOM 1477 CG2 VAL 353
                                 9.384 -14.703 10.349 1.00 18.40
                                9.853 -16.938 7.237 1.00 15.38
     ATOM 1478 C VAL 353
                                10.850 -16.773 6.525 1.00 18.40
     ATOM 1479 O VAL 353
25
     ATOM 1480 N ASN 354
                                9.183 -18.086 7.298 1.00 14.74
                                 9.578 -19.259 6.521 1.00 14.74
     ATOM 1481 CA ASN 354
     ATOM 1482 CB ASN 354
                                 8.640 -20.435 6.799 1.00 19.97
     ATOM 1483 CG ASN 354
                                 8.832 -21.020 8.180 1.00 19.97
                                 9.879 - 20.848 8.799 1.00 19.97
     ATOM 1484 OD1 ASN 354
30
     ATOM 1485 ND2 ASN 354
                                  7.826 -21.734 8.664 1.00 19.97
     ATOM 1486 C ASN 354
                                9.550 -18.939 5.034 1.00 14.74
     ATOM 1487 O ASN 354
                                10.452 -19.319 4.290 1.00 19.97
                               8.507 -18.230 4.613 1.00 13.03
     ATOM 1488 N HIS 355
                                8.329 -17.837 3.220 1.00 13.03
     ATOM 1489 CA HIS 355
35
                                6.960 -17.164 3.042 1.00 24.39
     ATOM 1490 CB HIS 355
                                6.753 -16.541 1.695 1.00 24.39
     ATOM 1491 CG HIS 355
                                7.195 -15.370 1.176 1.00 24.39
     ATOM 1492 CD2 HIS 355
                                 ATOM 1493 ND1 HIS 355
                                 6.005 -16.368 -0.372 1.00 24.39
     ATOM 1494 CE1 HIS 355
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                                 6.720 -15.289 -0.107 1.00 24.39
     ATOM 1495 NE2 HIS 355
                               9.434 -16.894 2.758 1.00 13.03
     ATOM 1496 C HIS 355
                               9.834 -16.920 1.595 1.00 24.39
     ATOM 1497 O HIS 355
     ATOM 1498 N ARG 356
                                9.878 -16.027 3.660 1.00 19.55
     ATOM 1499 CA ARG 356
                                 10.920 -15.054 3.358 1.00 19.55
45
                                 10.970 -14.001 4.460 1.00 22.01
     ATOM 1500 CB ARG 356
     ATOM 1501 CG ARG 356
                                 9.772 -13.081 4.454 1.00 22.01
     ATOM 1502 CD ARG 356
                                 10.097 -11.784 3.750 1.00 22.01
                                 10.932 -10.934 4.592 1.00 22.01
     ATOM 1503 NE ARG 356
                                 11.822 -10.059 4.137 1.00 22.01
     ATOM 1504 CZ ARG 356
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12.010 -9.907 2.833 1.00 22.01
    ATOM 1505 NH1 ARG 356
    ATOM 1506 NH2 ARG 356
                                 12.519 -9.325 4.992 1.00 22.01
                                12,297 -15.675 3.158 1.00 19.55
    ATOM 1507 C ARG 356
                                13.127 -15.126 2.434 1.00 22.01
    ATOM 1508 O ARG 356
                               12.547 -16.788 3.841 1.00 23.18
    ATOM 1509 N LYS 357
                                13.815 -17.504 3.739 1.00 23.18
    ATOM 1510 CA LYS 357
                                13.879 - 18.273 2.415 1.00 42.91
    ATOM 1511 CB LYS 357
                                12.750 -19.277 2.274 1.00 42.91
     ATOM 1512 CG LYS 357
                                12.773 -20.021 0.960 1.00 42.91
    ATOM 1513 CD LYS 357
     ATOM 1514 CE LYS 357
                                11.619 -21.011 0.913 1.00 42.91
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                                11.629 -21.845 -0.316 1.00 42.91
     ATOM 1515 NZ LYS 357
                               15.047 -16.619 3.918 1.00 23.18
     ATOM 1516 C LYS 357
     ATOM 1517 O LYS 357
                               15.816 -16.396 2.982 1.00 42.91
                               15.228 -16.122 5.137 1.00 32.39
     ATOM 1518 N HIS 358
                               16.367 -15.272 5.460 1.00 32.39
     ATOM 1519 CA HIS 358
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                                16.181 -14.626 6.835 1.00 26.77
     ATOM 1520 CB HIS 358
                                15.232 -13.468 6.841 1.00 26.77
     ATOM 1521 CG HIS 358
                                15.452 -12.138 6.709 1.00 26.77
     ATOM 1522 CD2 HIS 358
     ATOM 1523 ND1 HIS 358
                                13.875 -13.615 7.028 1.00 26.77
                                13.300 -12.426 7.012 1.00 26.77
     ATOM 1524 CE1 HIS 358
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     ATOM 1525 NE2 HIS 358
                                14.234 -11.513 6.821 1.00 26.77
                               17.633 -16.115 5.480 1.00 32.39
     ATOM 1526 C HIS 358
     ATOM 1527 O HIS 358
                               17.618 -17.248 5.961 1.00 26.77
                                18.728 -15.561 4.972 1.00 41.97
     ATOM 1528 N ASN 359
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     ATOM 1529 CA ASN 359
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     ATOM 1530 CB ASN 359
                                20.663 -16.134 6.331 1.00 41.97
     ATOM 1531 C ASN 359
                                21.821 -15.731 6.436 1.00 46.84
     ATOM 1532 O ASN 359
                               19.908 -16.450 7.379 1.00 35.72
     ATOM 1533 N ILE 360
                                20.394 -16.359 8.753 1.00 35.72
     ATOM 1534 CA ILE 360
30
                                19.819 -15.113 9.480 1.00 36.14
     ATOM 1535 CB ILE 360
                                20.327 -15.050 10.918 1.00 36.14
     ATOM 1536 CG2 ILE 360
                                20.204 -13.833 8.734 1.00 36.14
     ATOM 1537 CG1 ILE 360
                                19.526 -12.591 9.265 1.00 36.14
     ATOM 1538 CD1 ILE 360
                               19.935 -17.611 9.493 1.00 35.72
     ATOM 1539 C ILE 360
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                               18.748 -17.953 9.479 1.00 36.14
     ATOM 1540 O ILE 360
                                20.877 -18.338 10.109 1.00 31.56
     ATOM 1541 N PRO 361
                                 22.334 -18.114 10.100 1.00 33.50
     ATOM 1542 CD PRO 361
     ATOM 1543 CA PRO 361
                                 20.532 -19.556 10.847 1.00 31.56
                                 21.901 -20.163 11.161 1.00 33.50
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     ATOM 1544 CB PRO 361
     ATOM 1545 CG PRO 361
                                 22.801 -18.967 11.249 1.00 33.50
     ATOM 1546 C PRO 361
                                19.743 -19.256 12.121 1.00 31.56
                                20.080 -18.338 12.867 1.00 33.50
     ATOM 1547 O PRO 361
                               18.688 -20.034 12.355 1.00 18.84
     ATOM 1548 N HIS 362
     ATOM 1549 CA HIS 362
                                17.840 -19.887 13.541 1.00 18.84
45
                                18.656 -20.151 14.812 1.00 31.38
     ATOM 1550 CB HIS 362
     ATOM 1551 CG HIS 362
                                19.540 -21.357 14.731 1.00 31.38
                                19.250 -22.667 14.537 1.00 31.38
     ATOM 1552 CD2 HIS 362
                                 20.910 -21.286 14.860 1.00 31.38
     ATOM 1553 ND1 HIS 362
                                21.427 -22.497 14.754 1.00 31.38
50
     ATOM 1554 CE1 HIS 362
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20.439 -23.353 14.558 1.00 31.38
    ATOM 1555 NE2 HIS 362
                               17.189 -18.506 13.628 1.00 18.84
     ATOM 1556 C HIS 362
                               16.980 -17.979 14.723 1.00 31.38
    ATOM 1557 O HIS 362
                                16.825 -17.950 12.476 1.00 18.69
    ATOM 1558 N PHE 363
                                16.209 -16.630 12.408 1.00 18.69
    ATOM 1559 CA PHE 363
                                15.825 -16.302 10.962 1.00 19.25
    ATOM 1560 CB PHE 363
    ATOM 1561 CG PHE 363
                                15.339 -14.894 10.765 1.00 19.25
                                 16.239 -13.862 10.530 1.00 19.25
     ATOM 1562 CD1 PHE 363
                                 13.981 -14.598 10.819 1.00 19.25
    ATOM 1563 CD2 PHE 363
                                 15.794 -12.556 10.351 1.00 19.25
    ATOM 1564 CE1 PHE 363
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                                 13.527 -13.296 10.642 1.00 19.25
     ATOM 1565 CE2 PHE 363
                                14.435 -12.273 10.407 1.00 19.25
     ATOM 1566 CZ PHE 363
                                14.995 -16.461 13.323 1.00 18.69
     ATOM 1567 C PHE 363
                                14.955 -15.540 14.138 1.00 19.25
     ATOM 1568 O PHE 363
                                14.016 -17.351 13.191 1.00 16.46
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     ATOM 1569 N TRP 364
                                12.797 -17.280 13.995 1.00 16.46
     ATOM 1570 CA TRP 364
                                11.882 -18.482 13.706 1.00 17.81
     ATOM 1571 CB TRP 364
                                10.588 -18.488 14.481 1.00 17.81
     ATOM 1572 CG TRP 364
     ATOM 1573 CD2 TRP 364
                                 9.586 -17.458 14.504 1.00 17.81
                                 8.547 -17.905 15.350 1.00 17.81
     ATOM 1574 CE2 TRP 364
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                                 9.467 -16.202 13.894 1.00 17.81
     ATOM 1575 CE3 TRP 364
                                 10.126 -19.486 15.290 1.00 17.81
     ATOM 1576 CD1 TRP 364
     ATOM 1577 NE1 TRP 364
                                 8.902 -19.144 15.814 1.00 17.81
                                 7.403 -17.142 15.602 1.00 17.81
     ATOM 1578 CZ2 TRP 364
                                 8.329 -15.444 14.145 1.00 17.81
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     ATOM 1579 CZ3 TRP 364
                                 7.312 -15.919 14.992 1.00 17.81
     ATOM 1580 CH2 TRP 364
                                13.046 -17.114 15.500 1.00 16.46
     ATOM 1581 C TRP 364
     ATOM 1582 O TRP 364
                                12.595 -16.133 16.087 1.00 17.81
                                13.779 -18.051 16.137 1.00 18.31
     ATOM 1583 N PRO 365
                                14.342 -19.314 15.625 1.00 25.61
     ATOM 1584 CD PRO 365
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                                 14.038 -17.920 17.577 1.00 18.31
     ATOM 1585 CA PRO 365
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     ATOM 1586 CB PRO 365
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     ATOM 1587 CG PRO 365
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     ATOM 1588 C PRO 365
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     ATOM 1589 O PRO 365
35
                                15.699 -16.207 17.112 1.00 25.16
     ATOM 1590 N LYS 366
                                 16.439 -14.968 17.338 1.00 25.16
     ATOM 1591 CA LYS 366
                                 17.537 -14.805 16.289 1.00 40.51
     ATOM 1592 CB LYS 366
                                 18.679 -15.792 16.417 1.00 40.51
     ATOM 1593 CG LYS 366
                                 19.664 -15.607 15.278 1.00 40.51
40
     ATOM 1594 CD LYS 366
                                 20.884 -16.492 15.440 1.00 40.51
     ATOM 1595 CE LYS 366
     ATOM 1596 NZ LYS 366
                                 21.800 -16.360 14.275 1.00 40.51
                                15.521 -13.747 17.317 1.00 25.16
     ATOM 1597 C LYS 366
                                15.593 -12.893 18.202 1.00 40.51
     ATOM 1598 O LYS 366
                                14.661 -13.666 16.307 1.00 25.30
     ATOM 1599 N LEU 367
45
                                 13.729 -12.551 16.184 1.00 25.30
     ATOM 1600 CA LEU 367
                                 12.989 -12.620 14.845 1.00 27.80
     ATOM 1601 CB LEU 367
     ATOM 1602 CG LEU 367
                                 11.964 -11.519 14.561 1.00 27.80
                                 12.621 -10.147 14.679 1.00 27.80
     ATOM 1603 CD1 LEU 367
                                 11.367 -11.724 13.175 1.00 27.80
50
     ATOM 1604 CD2 LEU 367
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12.730 -12.596 17.332 1.00 25.30
    ATOM 1605 C LEU 367
                               12.337 -11.563 17.877 1.00 27.80
     ATOM 1606 O LEU 367
                               12.345 -13.807 17.712 1.00 26.12
    ATOM 1607 N LEU 368
                                11.396 -14.019 18.793 1.00 26.12
     ATOM 1608 CA LEU 368
                                11.105 -15.515 18.919 1.00 33.27
     ATOM 1609 CB LEU 368
    ATOM 1610 CG LEU 368
                                9.696 -15.976 19.289 1.00 33.27
                                 8.640 -15.182 18.529 1.00 33.27
    ATOM 1611 CD1 LEU 368
                                 9.582 -17.460 18.976 1.00 33.27
    ATOM 1612 CD2 LEU 368
     ATOM 1613 C LEU 368
                               11.973 -13.466 20.096 1.00 26.12
    ATOM 1614 O LEU 368
                               11.249 -12.920 20.930 1.00 33.27
10
     ATOM 1615 N MET 369
                                13.289 -13.571 20.244 1.00 24.39
                                13.971 -13.076 21.432 1.00 24.39
     ATOM 1616 CA MET 369
                                15.382 -13.656 21.511 1.00 47.44
     ATOM 1617 CB MET 369
                                 15.407 -15.096 22.009 1.00 47.44
     ATOM 1618 CG MET 369
                                16.850 -16.029 21.464 1.00 47.44
    ATOM 1619 SD MET 369
15
     ATOM 1620 CE MET 369
                                18.186 -15.114 22.246 1.00 47.44
                                13.996 -11.552 21.491 1.00 24.39
     ATOM 1621 C MET 369
                                14.212 -10.971 22.557 1.00 47.44
     ATOM 1622 O MET 369
     ATOM 1623 N LYS 370
                               13.749 -10.904 20.354 1.00 27.31
                                13.713 -9.445 20.297 1.00 27.31
     ATOM 1624 CA LYS 370
20
     ATOM 1625 CB LYS 370
                                13.739 -8.951 18.847 1.00 28.20
                                15.004 -9.312 18.090 1.00 28.20
     ATOM 1626 CG LYS 370
                                16.231 -8.810 18.824 1.00 28.20
     ATOM 1627 CD LYS 370
                                17.512 -9.244 18.142 1.00 28.20
     ATOM 1628 CE LYS 370
                                18.696 -8.851 18.952 1.00 28.20
25
     ATOM 1629 NZ LYS 370
     ATOM 1630 C LYS 370
                               12.453 -8.945 21.002 1.00 27.31
                               12.424 -7.835 21.535 1.00 28.20
     ATOM 1631 O LYS 370
                                11.413 -9.776 21.009 1.00 26.41
     ATOM 1632 N VAL 371
     ATOM 1633 CA VAL 371
                                 10.157 -9.432 21.668 1.00 26.41
                                 9.109 -10.561 21.512 1.00 25.61
     ATOM 1634 CB VAL 371
30
                                 7.825 -10.205 22.245 1.00 25.61
     ATOM 1635 CG1 VAL 371
                                  8.819 -10.805 20.044 1.00 25.61
     ATOM 1636 CG2 VAL 371
                                10.450 -9.205 23.151 1.00 26.41
     ATOM 1637 C VAL 371
     ATOM 1638 O VAL 371
                                9.962 -8.248 23.752 1.00 25.61
                                11.294 -10.065 23.713 1.00 26.28
     ATOM 1639 N THR 372
35
                                 11.683 -9.972 25.116 1.00 26.28
     ATOM 1640 CA THR 372
                                 12.656 -11.109 25.500 1.00 28.14
     ATOM 1641 CB THR 372
                                 12.025 -12.377 25.275 1.00 28.14
     ATOM 1642 OG1 THR 372
                                 13.055 -11.001 26.965 1.00 28.14
     ATOM 1643 CG2 THR 372
                                12.358 -8.624 25.372 1.00 26.28
     ATOM 1644 C THR 372
40
     ATOM 1645 O THR 372
                                12.047 -7.937 26.350 1.00 28.14
                                13.269 -8.247 24.478 1.00 15.09
     ATOM 1646 N ASP 373
                                13.977 -6.979 24.588 1.00 15.09
     ATOM 1647 CA ASP 373
     ATOM 1648 CB ASP 373
                                14.976 -6.822 23.435 1.00 37.94
     ATOM 1649 CG ASP 373
                                16.065 -7.893 23.445 1.00 37.94
45
                                 16.248 -8.571 24.483 1.00 37.94
     ATOM 1650 OD1 ASP 373
                                 16.750 -8.052 22.410 1.00 37.94
     ATOM 1651 OD2 ASP 373
     ATOM 1652 C ASP 373
                                12.969 -5.833 24.577 1.00 15.09
                                13.040 -4.928 25.407 1.00 37.94
     ATOM 1653 O ASP 373
     ATOM 1654 N LEU 374
                                12.008 -5.901 23.659 1.00 17.04
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10.974 -4.880 23.549 1.00 17.04
     ATOM 1655 CA LEU 374
     ATOM 1656 CB LEU 374
                                10.071 -5.155 22.344 1.00 20.58
                                10.624 -4.720 20.985 1.00 20.58
    ATOM 1657 CG LEU 374
                                 9.826 -5.352 19.862 1.00 20.58
     ATOM 1658 CD1 LEU 374
     ATOM 1659 CD2 LEU 374
                                 10.599 -3.202 20.882 1.00 20.58
                               10.145 -4.786 24.825 1.00 17.04
     ATOM 1660 C LEU 374
                                9.783 -3.688 25.256 1.00 20.58
     ATOM 1661 O LEU 374
                                9.850 -5.935 25.430 1.00 20.46
     ATOM 1662 N ARG 375
                                 9.080 -5.977 26.673 1.00 20.46
     ATOM 1663 CA ARG 375
                                 8.873 -7.422 27.140 1.00 55.89
     ATOM 1664 CB ARG 375
10
                                 8.180 -8.354 26.152 1.00 55.89
     ATOM 1665 CG ARG 375
                                 6.692 -8.084 26.027 1.00 55.89
     ATOM 1666 CD ARG 375
     ATOM 1667 NE ARG 375
                                 5.943 -9.338 25.968 1.00 55.89
                                 5.054 -9.654 25.028 1.00 55.89
     ATOM 1668 CZ ARG 375
                                 4.782 -8.808 24.040 1.00 55.89
     ATOM 1669 NH1 ARG 375
15
                                  4.438 -10.829 25.073 1.00 55.89
     ATOM 1670 NH2 ARG 375
                                9.874 -5.221 27.735 1.00 20.46
     ATOM 1671 C ARG 375
                                9.328 -4.391 28.463 1.00 55.89
     ATOM 1672 O ARG 375
     ATOM 1673 N MET 376
                                11.174 -5.502 27.794 1.00 20.10
                                12.076 -4.863 28.744 1.00 20.10
     ATOM 1674 CA MET 376
20
                                13.493 -5.417 28.580 1.00 63.73
     ATOM 1675 CB MET 376
                                 13.956 -6.310 29.722 1.00 63.73
     ATOM 1676 CG MET 376
     ATOM 1677 SD MET 376
                                14.494 -5.373 31.182 1.00 63.73
                                12.934 -5.151 32.087 1.00 63.73
     ATOM 1678 CE MET 376
                                12.081 -3.347 28.566 1.00 20.10
25
     ATOM 1679 C MET 376
     ATOM 1680 O MET 376
                                11.973 -2.602 29.539 1.00 63.73
                               12.194 -2.896 27.321 1.00 30.02
     ATOM 1681 N ILE 377
                                12.198 -1.469 27.014 1.00 30.02
     ATOM 1682 CA ILE 377
     ATOM 1683 CB ILE 377
                               12.329 -1.228 25.488 1.00 19.31
                                12.088 0.242 25.152 1.00 19.31
     ATOM 1684 CG2 ILE 377
30
                                13.711 -1.685 25.011 1.00 19.31
     ATOM 1685 CG1 ILE 377
                                13.906 -1.634 23.507 1.00 19.31
     ATOM 1686 CD1 ILE 377
     ATOM 1687 C ILE 377
                               10.915 -0.821 27.542 1.00 30.02
                               10.962 0.216 28.211 1.00 19.31
     ATOM 1688 O ILE 377
                                9.779 -1.455 27.266 1.00 21.85
     ATOM 1689 N GLY 378
35
                                 8.505 -0.936 27.729 1.00 21.85
     ATOM 1690 CA GLY 378
                                8.459 -0.821 29.243 1.00 21.85
     ATOM 1691 C GLY 378
                                7.990 0.185 29.779 1.00 34.01
     ATOM 1692 O GLY 378
                                8.967 -1.842 29.928 1.00 31.30
     ATOM 1693 N ALA 379
                                 8.996 -1.870 31.388 1.00 31.30
40
     ATOM 1694 CA ALA 379
                                 9.471 -3.231 31.880 1.00 30.06
     ATOM 1695 CB ALA 379
     ATOM 1696 C ALA 379
                                9.895 -0.763 31.938 1.00 31.30
                                9.482 0.002 32.810 1.00 30.06
     ATOM 1697 O ALA 379
                                11.117 -0.677 31.418 1.00 28.61
     ATOM 1698 N CYS 380
     ATOM 1699 CA CYS 380
                                12.067 0.349 31.841 1.00 28.61
45
                                13.360 0.268 31.025 1.00 60.26
     ATOM 1700 CB CYS 380
                                14.499 -1.067 31.470 1.00 60.26
     ATOM 1701 SG CYS 380
     ATOM 1702 C CYS 380
                                11.449 1.730 31.658 1.00 28.61
                               11.516 2.573 32.554 1.00 60.26
     ATOM 1703 O CYS 380
                               10.840 1.957 30.498 1.00 30.42
50
     ATOM 1704 N HIS 381
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ATOM 1705 CA HIS 381
                               10.212 3.243 30.216 1.00 30.42
                               9.696 3.306 28.779 1.00 16.49
    ATOM 1706 CB HIS 381
                               8.942 4.562 28.472 1.00 16.49
    ATOM 1707 CG HIS 381
                                9.370 5.805 28.151 1.00 16.49
    ATOM 1708 CD2 HIS 381
                                7.566 4.633 28.524 1.00 16.49
    ATOM 1709 ND1 HIS 381
                               7.180 5.866 28.251 1.00 16.49
    ATOM 1710 CE1 HIS 381
    ATOM 1711 NE2 HIS 381
                                8.255 6.596 28.021 1.00 16.49
                              9.073 3.539 31.182 1.00 30.42
    ATOM 1712 C HIS 381
                              8.856 4.690 31.552 1.00 16.49
    ATOM 1713 O HIS 381
                               8.330 2.506 31.564 1.00 22.89
    ATOM 1714 N ALA 382
10
                                7.218 2.666 32.493 1.00 22.89
    ATOM 1715 CA ALA 382
                                6.520 1.336 32.708 1.00 34.50
    ATOM 1716 CB ALA 382
                               7.738 3.213 33.819 1.00 22.89
    ATOM 1717 C ALA 382
                               7.219 4.200 34.343 1.00 34.50
    ATOM 1718 O ALA 382
                               8.789 2.586 34.336 1.00 26.39
    ATOM 1719 N SER 383
15
     ATOM 1720 CA SER 383
                               9.400 3.006 35.591 1.00 26.39
                               10.510 2.030 35.985 1.00 52.94
    ATOM 1721 CB SER 383
                               10.015 0.702 36.046 1.00 52.94
     ATOM 1722 OG SER 383
                               9.966 4.418 35.470 1.00 26.39
     ATOM 1723 C SER 383
                               9.772 5.253 36.357 1.00 52.94
20
     ATOM 1724 O SER 383
                               10.662 4.683 34.368 1.00 30.36
    ATOM 1725 N ARG 384
     ATOM 1726 CA ARG 384
                               11.249 5.995 34.134 1.00 30.36
                                12.116 5.977 32.874 1.00 37.39
     ATOM 1727 CB ARG 384
                                12.601 7.344 32.431 1.00 37.39
     ATOM 1728 CG ARG 384
     ATOM 1729 CD ARG 384
                                14.070 7.321 32.060 1.00 37.39
25
                                14.935 7.597 33.204 1.00 37.39
     ATOM 1730 NE ARG 384
                                15.750 8.646 33.291 1.00 37.39
     ATOM 1731 CZ ARG 384
                                15.824 9.529 32.303 1.00 37.39
     ATOM 1732 NH1 ARG 384
                                16.488 8.819 34.376 1.00 37.39
     ATOM 1733 NH2 ARG 384
                               10.169 7.067 34.030 1.00 30.36
30
     ATOM 1734 C ARG 384
                               10.301 8.144 34.616 1.00 37.39
     ATOM 1735 O ARG 384
                               9.078 6.749 33.338 1.00 24.47
     ATOM 1736 N PHE 385
                                7.980 7.693 33.171 1.00 24.47
     ATOM 1737 CA PHE 385
                                6.859 7.092 32.319 1.00 28.70
     ATOM 1738 CB PHE 385
                                5.710 8.036 32.075 1.00 28.70
     ATOM 1739 CG PHE 385
35
                                5.795 9.017 31.092 1.00 28.70
     ATOM 1740 CD1 PHE 385
                                4.549 7.954 32.836 1.00 28.70
     ATOM 1741 CD2 PHE 385
     ATOM 1742 CE1 PHE 385
                                4.740 9.903 30.874 1.00 28.70
     ATOM 1743 CE2 PHE 385
                                3.491 8.835 32.624 1.00 28.70
40
     ATOM 1744 CZ PHE 385
                                3.587 9.812 31.641 1.00 28.70
     ATOM 1745 C PHE 385
                               7.436 8.097 34.533 1.00 24.47
                               7.250 9.285 34.805 1.00 28.70
     ATOM 1746 O PHE 385
                               7.208 7.107 35.391 1.00 31.13
     ATOM 1747 N LEU 386
                                6.690 7.352 36.734 1.00 31.13
     ATOM 1748 CA LEU 386
                                6.596 6.044 37.513 1.00 39.10
     ATOM 1749 CB LEU 386
45
                               7.577 8.348 37.474 1.00 31.13
     ATOM 1750 C LEU 386
                               7.085 9.201 38.217 1.00 39.10
     ATOM 1751 O LEU 386
                               8.884 8.254 37.243 1.00 36.46
     ATOM 1752 N HIS 387
                               9.837 9.152 37.881 1.00 36.46
     ATOM 1753 CA HIS 387
     ATOM 1754 CB HIS 387
                               11.258 8.589 37.794 1.00 62.78
50
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11.459 7.338 38.590 1.00 62.78
    ATOM 1755 CG HIS 387
                               10.601 6.614 39.346 1.00 62.78
    ATOM 1756 CD2 HIS 387
                               12.675 6.689 38.663 1.00 62.78
    ATOM 1757 ND1 HIS 387
                               12.554 5.620 39.431 1.00 62.78
    ATOM 1758 CE1 HIS 387
    ATOM 1759 NE2 HIS 387
                               11.309 5.550 39.856 1.00 62.78
 5
    ATOM 1760 C HIS 387
                               9.778 10.544 37.266 1.00 36.46
                               9.885 11.543 37.979 1.00 62.78
    ATOM 1761 O HIS 387
                               9.587 10.612 35.950 1.00 33.41
    ATOM 1762 N MET 388
    ATOM 1763 CA MET 388
                                9.505 11.894 35.258 1.00 33.41
                                9.269 11.703 33.755 1.00 42.63
    ATOM 1764 CB MET 388
10
                                10,456 11.144 32.982 1.00 42.63
    ATOM 1765 CG MET 388
                                10.253 11.325 31.192 1.00 42.63
    ATOM 1766 SD MET 388
    ATOM 1767 CE MET 388
                                9.501 9.772 30.748 1.00 42.63
                               8.385 12.746 35.849 1.00 33.41
    ATOM 1768 C MET 388
                               8.573 13.934 36.103 1.00 42.63
    ATOM 1769 O MET 388
15
                               7.235 12.126 36.092 1.00 39.26
    ATOM 1770 N LYS 389
    ATOM 1771 CA LYS 389
                                6.082 12.825 36.659 1.00 39.26
                                4.867 11.900 36.719 1.00 52.87
    ATOM 1772 CB LYS 389
                                4.237 11.594 35.379 1.00 52.87
    ATOM 1773 CG LYS 389
                                3.048 10.667 35.553 1.00 52.87
    ATOM 1774 CD LYS 389
20
                                3.482 9.327 36.125 1.00 52.87
    ATOM 1775 CE LYS 389
                                2.335 8.407 36.326 1.00 52.87
     ATOM 1776 NZ LYS 389
                               6.363 13.360 38.056 1.00 39.26
     ATOM 1777 C LYS 389
                               5.837 14.404 38.452 1.00 52.87
     ATOM 1778 O LYS 389
    ATOM 1779 N VAL 390
                                7.156 12.614 38.818 1.00 44.18
25
                                7.508 13.016 40.172 1.00 44.18
    ATOM 1780 CA VAL 390
                                8.299 11.898 40.905 1.00 50.50
     ATOM 1781 CB VAL 390
                                8.718 12.362 42.293 1.00 50.50
     ATOM 1782 CG1 VAL 390
     ATOM 1783 CG2 VAL 390
                                 7.455 10.640 41.012 1.00 50.50
                                8.352 14.288 40.145 1.00 44.18
     ATOM 1784 C VAL 390
30
                                8.144 15.198 40.948 1.00 50.50
     ATOM 1785 O VAL 390
                                9.261 14.368 39.179 1.00 38.64
     ATOM 1786 N GLU 391
     ATOM 1787 CA GLU 391
                                10.161 15.509 39.056 1.00 38.64
                                11.483 15.060 38.424 1.00 64.18
     ATOM 1788 CB GLU 391
                                12.065 13.766 39.009 1.00 64.18
     ATOM 1789 CG GLU 391
35
                                12.662 13.922 40.405 1.00 64.18
     ATOM 1790 CD GLU 391
                                12.190 14.773 41.192 1.00 64.18
     ATOM 1791 OE1 GLU 391
                                13.611 13.173 40.721 1.00 64.18
     ATOM 1792 OE2 GLU 391
                                9.623 16.737 38.314 1.00 38.64
     ATOM 1793 C GLU 391
     ATOM 1794 O GLU 391
                                9.656 17.850 38.849 1.00 64.18
40
                                9.125 16.539 37.096 1.00 37.24
     ATOM 1795 N CYS 392
     ATOM 1796 CA CYS 392
                                8.611 17.635 36.271 1.00 37.24
                                8.879 17.345 34.784 1.00 30.64
     ATOM 1797 CB CYS 392
                                10.634 17.137 34.283 1.00 30.64
     ATOM 1798 SG CYS 392
     ATOM 1799 C CYS 392
                               7.110 17.882 36.496 1.00 37.24
45
                                6.403 17.011 37.006 1.00 30.64
     ATOM 1800 O CYS 392
     ATOM 1801 N PRO 393
                                6.625 19.107 36.199 1.00 40.56
                                7.444 20.297 35.904 1.00 33.41
     ATOM 1802 CD PRO 393
                              5.209 19.473 36.358 1.00 40.56
     ATOM 1803 CA PRO 393
                              5.253 21.001 36.404 1.00 33.41
     ATOM 1804 CB PRO 393
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6.409 21.332 35.527 1.00 33.41
    ATOM 1805 CG PRO 393
                               4.330 18.975 35.207 1.00 40.56
    ATOM 1806 C PRO 393
                               4.776 18.907 34.057 1.00 33.41
    ATOM 1807 O PRO 393
                               3.067 18.691 35.516 1.00 41.91
    ATOM 1808 N THR 394
                                2.101 18.186 34.540 1.00 41.91
    ATOM 1809 CA THR 394
                                0.691 18.075 35.156 1.00 62.04
    ATOM 1810 CB THR 394
                                 0.706 18.582 36.497 1.00 62.04
    ATOM 1811 OG1 THR 394
                                 0.232 16.626 35.168 1.00 62.04
    ATOM 1812 CG2 THR 394
    ATOM 1813 C THR 394
                               1.995 18.984 33.242 1.00 41.91
                                1.758 18.411 32.181 1.00 62.04
    ATOM 1814 O THR 394
10
                                2.191 20.297 33.327 1.00 43.92
    ATOM 1815 N GLU 395
                                2.104 21.176 32.160 1.00 43.92
    ATOM 1816 CA GLU 395
    ATOM 1817 CB GLU 395
                                2.313 22.626 32.585 1.00 34.22
                               3.071 20.814 31.031 1.00 43.92
    ATOM 1818 C GLU 395
                                2.887 21.243 29.891 1.00 34.22
    ATOM 1819 O GLU 395
15
    ATOM 1820 N LEU 396
                               4.104 20.041 31.350 1.00 34.92
                                5.096 19.634 30.359 1.00 34.92
     ATOM 1821 CA LEU 396
                                6.473 19.495 31.017 1.00 35.81
     ATOM 1822 CB LEU 396
                                7.074 20.747 31.662 1.00 35.81
     ATOM 1823 CG LEU 396
                                 8.427 20.410 32.263 1.00 35.81
     ATOM 1824 CD1 LEU 396
20
                                 7.209 21.857 30.629 1.00 35.81
     ATOM 1825 CD2 LEU 396
                               4.731 18.324 29.661 1.00 34.92
     ATOM 1826 C LEU 396
                               5.343 17.954 28.659 1.00 35.81
     ATOM 1827 O LEU 396
                               3.734 17.627 30.197 1.00 35.28
     ATOM 1828 N PHE 397
                                3.302 16.352 29.640 1.00 35.28
     ATOM 1829 CA PHE 397
25
                                3.059 15.341 30.764 1.00 27.13
     ATOM 1830 CB PHE 397
                                4.285 15.004 31.561 1.00 27.13
     ATOM 1831 CG PHE 397
                                 4.700 15.824 32.604 1.00 27.13
     ATOM 1832 CD1 PHE 397
     ATOM 1833 CD2 PHE 397
                                 5.021 13.860 31.273 1.00 27.13
                                 5.831 15.510 33.349 1.00 27.13
     ATOM 1834 CE1 PHE 397
30
                                 6.155 13.537 32.013 1.00 27.13
     ATOM 1835 CE2 PHE 397
                                6.561 14.364 33.052 1.00 27.13
     ATOM 1836 CZ PHE 397
                               2.027 16.474 28.812 1.00 35.28
     ATOM 1837 C PHE 397
                               0.977 16.861 29.331 1.00 27.13
     ATOM 1838 O PHE 397
                                2.102 16.164 27.505 1.00 26.41
     ATOM 1839 N PRO 398
35
                                3.305 15.850 26.713 1.00 19.32
     ATOM 1840 CD PRO 398
                                0.917 16.247 26.647 1.00 26.41
     ATOM 1841 CA PRO 398
     ATOM 1842 CB PRO 398
                                1.439 15.752 25.300 1.00 19.32
     ATOM 1843 CG PRO 398
                                2.867 16.193 25.312 1.00 19.32
     ATOM 1844 C PRO 398
                               -0.157 15.313 27.206 1.00 26.41
40
                                0.160 14.232 27.710 1.00 19.32
     ATOM 1845 O PRO 398
                               -1.439 15.702 27.104 1.00 25.12
     ATOM 1846 N PRO 399
                                -1.935 16.929 26.454 1.00 24.32
     ATOM 1847 CD PRO 399
     ATOM 1848 CA PRO 399
                                -2.554 14.894 27.612 1.00 25.12
                                -3.777 15.594 27.022 1.00 24.32
     ATOM 1849 CB PRO 399
45
                                -3.349 17.026 26.974 1.00 24.32
     ATOM 1850 CG PRO 399
     ATOM 1851 C PRO 399
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                               -2.599 12.540 28.085 1.00 24.32
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     ATOM 1854 CA LEU 400
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    ATOM 1858 CD2 LEU 400
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    ATOM 1860 O LEU 400
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     ATOM 1863 CB PHE 401
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    ATOM 1864 CG PHE 401
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     ATOM 1866 CD2 PHE 401
    ATOM 1867 CE1 PHE 401
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     ATOM 1874 CB LEU 402
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     ATOM 1876 CD1 LEU 402
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     ATOM 1881 CA GLU 403
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     ATOM 1886 OE2 GLU 403
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     ATOM 1893 CG2 VAL 404
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     ATOM 1897 CA PHE 405
     ATOM 1898 CB PHE 405
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     ATOM 1899 CG PHE 405
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     ATOM 1901 CD2 PHE 405
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     ATOM 1902 CE1 PHE 405
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                                 0.090 6.434 32.107 1.00 34.35
    ATOM 1907 OXT PHE 405
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                              10.048 8.688 23.016 1.00 33.36
    ATOM 1909 C2 TRI
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    ATOM 1910 C3 TRI
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    ATOM 1911 C4 TRI
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    ATOM 1914 C7 TRI
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    ATOM 1916 C9 TRI
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    ATOM 1917 C10 TRI
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    ATOM 1918 C11 TRI
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                               9.125 7.756 23.490 1.00 33.36
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    ATOM 1924 I3 TRI 1
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                              9.407 6.654 15.852 1.00 35.85
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                              8.798 8.969 26.979 1.00 33.36
     ATOM 1927 O1 TRI
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     ATOM 1928 O4 TRI 1
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     ATOM 1932 O1 HOH 534
     ATOM 1933 O1 HOH 538
                                4.845 14.369 13.635 1.00 33.36
     ATOM 1934 O1 HOH 540
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     ATOM 1937 O1 HOH 556
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     ATOM 1941 O4 CAD 701
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                                0.592 2.019 1.654 1.00 28.02
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                                                              AS
                               16.338 -1.161 29.914 1.00 37.00
                                                              AS
     ATOM 1944 AS AS
                         802
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                              -14.931 -11.763 25.324 1.00 37.00
     ATOM 1945 AS AS
                         803
                                                              AS
     END
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PCT/US98/25296 WO 99/26966

## APPENDIX 5

## TR IPBR2.PDB

REMARK rTR ipbr2 full length numbering REMARK REMARK Rfactor 0.214 Rfree 0.224 5 REMARK Resolution 15. 2.2 all reflections **REMARK** REMARK Three cacodylate-modified cysteines (CYA) REMARK Cya334, Cya380, Cya392 10 REMARK cacodylate modeled as single arsenic atom **REMARK** REMARK side chain of certain residues modeled as ALA due to poor REMARK however, residue name reflects true residue for clarity 15 REMARK REMARK clone obtained from Murray et. al. REMARK deposited sequence confirmed, REMARK differing from that reported by Thompson et. al. REMARK in the following codons: 20 REMARK 281 Thr - Ala REMARK 285 Lys - Glu REMARK identical to that reported by Mitsuhashi et. al. REMARK gb:RNTRAVI X07409 M.B. MURRAY, N.D.ZILZ, JRNL AUTH 25 N.L.MCCREARY, M.J.MACDONALD JRNL **AUTH 2 H.C.TOWLE** TITL ISOLATION AND CHARACTERIZATION OF RAT CDNA JRNL **CLONES FOR** TWO TITL 2 DISTINCT THYROID HORMONE RECPTORS 30 JRNL V. 263 25 1988 JRNL REF JBC AUTH C.C.THOMPSON, C.WEINBERGER, R.LEBO, R.M.EVANS JRNL TITL IDENTIFICATION OF A NOVEL THYROID HORMONE JRNL RECEPTOR 35 **EXPRESSED** TITL 2 IN THE MAMMALIAN CENTRAL NERVOUS SYSTEM JRNL. V. 237 1987 JRNL REF SCIENCE AUTH T.MITSUHASHI, G.TENNYSON, V.NIKODEM JRNL JRNL TITL NUCLEOTIDE SEQUENCE OF NOVEL CDNAS GENERATED 40 BY**ALTERNATIVE** 

TITL 2 SPLICING OF A RAT THYROID HORMONE RECEPTOR JRNL **GENE** 

V. 16 12 1988

TRANSCRIPT REF NUC. ACIDS. RES. JRNL

45

REMARK 1 CB ARG 157 68.481 10.663 6.906 1.00 57.50 ATOM 2 CG ARG 157 69.793 10.213 7.512 1.00 59.93 ATOM

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70.510 11.365 8.189 1.00 70.24
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             4 NE ARG 157
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                               71.599 10.492 10.224 1.00 78.75
    ATOM
             5 CZ ARG 157
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    ATOM
             6 NH1 ARG 157
             7 NH2 ARG 157
                               72.697 10.075 10.839 1.00 83.44
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             8 C ARG 157
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             15 CB PRO 158
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             31 CB PRO 160
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             47 C PRO 162
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     ATOM
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             76 CZ2 TRP 165
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     ATOM
             78 CH2 TRP 165
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                               53.269 21.943 4.537 1.00 23.35
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             84 CG ASP 166
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             86 OD2 ASP 166
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             91 CB LEU 167
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             94 CD2 LEU 167
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             97 N ILE 168
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            112 NE2 HIS 169
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            117 CB VAL 170
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            119 CG2 VAL 170
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            121 O VAL 170
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            124 CB ALA 171
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            129 CB THR 172
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            132 C THR 172
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                              59.346 31.815 6.360 1.00 23.54
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            133 O THR 172
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            134 N GLU 173
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                               54.679 32.974 4.207 1.00 40.39
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            143 N ALA 174
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            144 CA ALA 174
            145 CB ALA 174
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                              57.097 33.847 9.338 1.00 23.47
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            147 O ALA 174
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            148 N HIS 175
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            150 CB HIS 175
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            151 CG HIS 175
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            152 CD2 HIS 175
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            155 NE2 HIS 175
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            159 CA ARG 176
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                               60.168 34.767 4.872 1.00 30.31
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                               61.286 33.793 4.576 1.00 39.36
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            161 CG ARG 176
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    ATOM 164 CZ ARG 176
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            165 NH1 ARG 176
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                               59.548 36.749 6.267 1.00 23.09
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                               60.163 37.807 6.173 1.00 30.71
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                              58.240 36.686 6.488 1.00 22.69
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            170 CA SER 177
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            171 CB SER 177
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                               55.507 36.611 7.331 1.00 27.68
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                              57.574 38.695 7.821 1.00 28.70
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            174 O SER 177
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                               58.540 38.850 10.060 1.00 21.88
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                               57.842 38.107 11.228 1.00 23.73
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            178 OG1 THR 178
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            179 CG2 THR 178
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            181 O THR 178
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            187 ND2 ASN 179
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                               63.653 43.390 10.346 1.00 29.96
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            194 O ALA 180
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                               64.266 43.163 7.057 1.00 37.15
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            196 CA GLN 181
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            197 CB GLN 181
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                                65.779 46.285 6.479 1.00 53.60
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                               66.531 39.363 4.477 1.00 49.98
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            207 O GLY 182
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    ATOM 209 CA SER 183
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            211 OG SER 183
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            212 C SER 183
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                              70.352 40.138 2.540 1.00 66.02
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                              68.453 41.338 2.413 1.00 60.68
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            215 CA HIS 184
                               69.131 42.600 2.139 1.00 60.01
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                               68.150 43.596 1.517 1.00 53.49
            216 CB HIS 184
    ATOM
                              69.798 43.209 3.380 1.00 59.43
           217 C HIS 184
     ATOM
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                              70.373 44.300 3.303 1.00 59.56
     ATOM 218 O HIS 184
            219 N TRP 185
                              69.753 42.500 4.508 1.00 57.54
     ATOM
                               70.343 42.995 5.754 1.00 54.25
     ATOM
            220 CA TRP 185
            221 CB TRP 185
                               70.147 41.988 6.899 1.00 47.54
     ATOM
                               70.905 40.692 6.752 1.00 41.08
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     ATOM
            222 CG TRP 185
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     ATOM
            223 CD2 TRP 185
     ATOM 224 CE2 TRP 185
                               72.522 39.070 6.874 1.00 30.27
                                73.202 41.146 7.919 1.00 35.23
     ATOM 225 CE3 TRP 185
                                70.462 39.553 6.149 1.00 39.73
     ATOM 226 CD1 TRP 185
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            227 NE1 TRP 185
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                                73.740 38.457 7.188 1.00 31.35
            228 CZ2 TRP 185
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                               74.416 40.535 8.230 1.00 32.76
            229 CZ3 TRP 185
     ATOM
                                74.673 39.203 7.861 1.00 31.71
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            230 CH2 TRP 185
            231 C TRP 185
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                               72.229 44.403 6.200 1.00 52.82
            232 O TRP 185
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                               72.605 42.584 4.938 1.00 54.57
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            233 N LYS 186
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            234 CA LYS 186
                               74.712 41.682 4.080 1.00 53.31
            235 CB LYS 186
     ATOM
                               74.338 44.160 4.061 1.00 58.96
            236 C LYS 186
     ATOM
            237 O LYS 186
                               75.417 44.731 4.226 1.00 62.57
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                               73.382 44.640 3.268 1.00 60.12
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            238 N GLN 187
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            239 CA GLN 187
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            240 CB GLN 187
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                               72.809 47.064 3.101 1.00 60.91
            241 C GLN 187
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                               73.149 48.213 2.822 1.00 66.50
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            242 O GLN 187
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            243 N ARG 188
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            244 CA ARG 188
     ATOM
                                69.504 47.462 4.466 1.00 55.21
            245 CB ARG 188
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     ATOM
            246 C ARG 188
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                               70.914 49.269 6.469 1.00 58.54
            247 O ARG 188
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     ATOM
                               72.202 47.432 6.607 1.00 55.46
            248 N ARG 189
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            249 CA ARG 189
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            250 CB ARG 189
                                73.211 46.437 8.619 1.00 47.73
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                                75.080 44.763 8.654 1.00 46.96
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            252 CD ARG 189
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            255 NH1 ARG 189
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                                78.600 43.860 8.148 1.00 67.84
            256 NH2 ARG 189
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            257 C ARG 189
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            258 O ARG 189
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            259 N LYS 190
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    ATOM 261 CB LYS 190
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            263 O LYS 190
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            265 CA PHE 191
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            266 CB PHE 191
    ATOM
                               79.170 49.336 11.123 1.00 49.51
    ATOM
            267 CG PHE 191
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                               78.828 49.124 9.791 1.00 52.20
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            268 CD1 PHE 191
                                80.029 48.437 11.748 1.00 47.25
    ATOM
            269 CD2 PHE 191
                               79.335 48.031 9.090 1.00 55.86
            270 CE1 PHE 191
    ATOM
            271 CE2 PHE 191
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                               80.195 47.139 9.727 1.00 51.55
            272 CZ PHE 191
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                              76.764 51.443 13.233 1.00 46.44
            273 C PHE 191
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                              76.647 52.645 12.996 1.00 51.28
    ATOM 274 O PHE 191
                              76.567 50.924 14.439 1.00 47.66
    ATOM 275 N LEU 192
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            276 CA LEU 192
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            277 CB LEU 192
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            278 CG LEU 192
                                74.180 52.339 17.871 1.00 28.17
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            280 CD2 LEU 192
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    ATOM
            281 C LEU 192
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                              78.604 52.024 16.008 1.00 41.65
            282 O LEU 192
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                               76.176 54.701 15.577 1.00 47.51
            284 CD PRO 193
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                               78.560 54.836 15.999 1.00 47.34
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            285 CA PRO 193
            286 CB PRO 193
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            287 CG PRO 193
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                              79.000 54.033 18.218 1.00 54.05
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                              80.783 54.383 16.891 1.00 50.63
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                               81.769 53.951 17.885 1.00 54.57
            291 CA ASP 194
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                               83.164 53.965 17.272 1.00 59.28
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            294 OD1 ASP 194
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            295 OD2 ASP 194
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            297 O ASP 194
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                              81.268 55.956 19.168 1.00 57.20
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                               81.206 56.775 20.371 1.00 59.68
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                               81.017 58.261 20.006 1.00 62.99
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            308 CB ILE 196
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                               75.701 54.195 21.560 1.00 42.11
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            309 CG2 ILE 196
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            315 CA GLY 197
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                               80.726 52.946 24.725 1.00 60.08
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            318 N GLN 198
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            320 CB GLN 198
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            323 N SER 199
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            324 CA SER 199
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            325 CB SER 199
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            331 CA PRO 200
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            340 CG1 ILE 201
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            341 CD1 ILE 201
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            343 O ILE 201
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            345 CA VAL 202
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            346 CB VAL 202
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            347 CG1 VAL 202
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            348 CG2 VAL 202
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            361 SD MET 204
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            369 CG PRO 205
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            374 CB ASP 206
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                                76.813 41.322 35.465 1.00 61.12
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             392 N LYS 209
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                                78.132 48.081 34.082 1.00 53.92
             393 CA LYS 209
     ATOM
                                79.034 49.236 34.515 1.00 49.71
             394 CB LYS 209
     ATOM
             395 C LYS 209
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                               77.767 47.945 31.711 1.00 45.62
             396 O LYS 209
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                                76.367 49.258 32.894 1.00 43.87
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             397 N VAL 210
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             398 CA VAL 210
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                                74.020 49.624 32.125 1.00 32.99
             399 CB VAL 210
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                                73.153 50.029 30.937 1.00 31.44
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             400 CG1 VAL 210
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             401 CG2 VAL 210
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                               75.868 51.061 31.234 1.00 43.30
             402 C VAL 210
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           405 CA ASP 211
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           406 CB ASP 211
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                               77.014 53.499 27.161 1.00 40.77
    ATOM 407 CG ASP 211
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           408 OD1 ASP 211
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                               78.111 53.549 26.574 1.00 37.49
           409 OD2 ASP 211
    ATOM
    ATOM 410 C ASP 211
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                              73.849 52.500 27.998 1.00 46.44
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           411 O ASP 211
           412 N LEU 212
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            413 CA LEU 212
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           414 CB LEU 212
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                               72.360 55.585 31.867 1.00 44.47
    ATOM 415 CG LEU 212
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           416 CD1 LEU 212
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                                71.217 54.634 32.153 1.00 45.94
           417 CD2 LEU 212
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                              72.325 54.886 28.049 1.00 40.77
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           419 O LEU 212
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           420 N GLU 213
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     ATOM 421 CA GLU 213
     ATOM 422 CB GLU 213
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                                75.598 57.848 23.722 1.00 59.23
     ATOM 424 CD GLU 213
     ATOM 425 OE1 GLU 213
                                75.655 58.939 23.121 1.00 60.14
                                76.611 57.158 23.980 1.00 64.78
     ATOM 426 OE2 GLU 213
                               72.913 54.810 25.066 1.00 42.63
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     ATOM 427 C GLU 213
                               72.008 54.779 24.226 1.00 37.04
     ATOM 428 O GLU 213
                               73.775 53.814 25.245 1.00 39.28
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     ATOM 430 CA ALA 214
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     ATOM 431 CB ALA 214
                               72.460 51.852 24.694 1.00 37.14
     ATOM 432 C ALA 214
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     ATOM 433 O ALA 214
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     ATOM 435 CA PHE 215
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     ATOM 436 CB PHE 215
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                               69.512 50.522 28.458 1.00 21.78
     ATOM 437 CG PHE 215
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                                69.553 49.171 28.771 1.00 24.64
     ATOM 438 CD1 PHE 215
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     ATOM 439 CD2 PHE 215
            440 CE1 PHE 215
                                68.429 48.528 29.277 1.00 27.63
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                                67.200 50.591 29.163 1.00 21.60
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            441 CE2 PHE 215
            442 CZ PHE 215
                               67.249 49.242 29.472 1.00 21.35
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                               69.675 51.706 25.694 1.00 35.75
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     ATOM
                               68.838 50.975 25.161 1.00 34.84
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            444 O PHE 215
            445 N SER 216
                               69.604 53.035 25.665 1.00 39.09
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                               68.506 53.739 25.001 1.00 40.61
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            447 CB SER 216
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                                68.616 55.603 26.537 1.00 68.66
            448 OG SER 216
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                               67.362 53.161 22.969 1.00 35.50
            450 O SER 216
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            451 N GLU 217
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            452 CA GLU 217
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                                70.881 55.315 19.925 1.00 53.25
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                                70.920 55.056 18.702 1.00 57.12
            456 OE1 GLU 217
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            457 OE2 GLU 217
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            458 C GLU 217
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            459 O GLU 217
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            460 N PHE 218
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            461 CA PHE 218
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                               69.743 48.392 22.925 1.00 29.10
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            462 CB PHE 218
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                                71.169 48.260 22.510 1.00 26.25
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            463 CG PHE 218
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            464 CD1 PHE 218
            465 CD2 PHE 218
                                71.510 48.233 21.163 1.00 23.53
     ATOM
                                73.504 48.072 23.073 1.00 27.68
            466 CE1 PHE 218
     ATOM
            467 CE2 PHE 218
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            468 CZ PHE 218
                               73.834 48.047 21.721 1.00 28.43
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                               67.445 49.202 22.321 1.00 31.30
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            469 C PHE 218
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            470 O PHE 218
                               66.726 48.496 21.621 1.00 35.18
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                                65.552 49.853 23.675 1.00 33.53
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            472 CA THR 219
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            473 CB THR 219
            474 OG1 THR 219
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                                65.797 49.562 26.145 1.00 34.32
            475 CG2 THR 219
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                               64.680 50.514 22.609 1.00 34.53
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            476 C THR 219
                               63.507 50.162 22.450 1.00 36.57
            477 O THR 219
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                               65.267 51.457 21.873 1.00 38.13
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            479 CA LYS 220
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            481 C LYS 220
                               64.140 51.182 19.716 1.00 41.80
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            482 O LYS 220
                               63.032 51.274 19.192 1.00 43.29
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            484 CA ILE 221
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            485 CB ILE 221
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            486 CG2 ILE 221
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            487 CG1 ILE 221
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            488 CD1 ILE 221
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                              64.141 47.922 18.845 1.00 40.49
            489 C ILE 221
     ATOM
            490 O ILE 221
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            491 N ILE 222
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            492 CA ILE 222
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            493 CB ILE 222
                               64.169 46.133 22.130 1.00 34.06
            494 CG2 ILE 222
                               63.287 46.881 23.130 1.00 26.15
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            495 CG1 ILE 222
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            496 CD1 ILE 222
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            497 C ILE 222
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            499 N THR 223
                               61.438 47.324 20.665 1.00 34.60
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            500 CA THR 223
            501 CB THR 223
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                               59.681 49.119 22.106 1.00 44.59
     ATOM
            502 OG1 THR 223
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            505 O THR 223
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            507 CD PRO 224
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            511 C PRO 224
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            512 O PRO 224
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            515 CB ALA 225
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            521 CG2 ILE 226
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            522 CG1 ILE 226
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            523 CD1 ILE 226
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            524 C ILE 226
            525 O ILE 226
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                               57.653 42.811 18.596 1.00 25.22
            526 N THR 227
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            527 CA THR 227
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            528 CB THR 227
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            529 OG1 THR 227
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            534 CA ARG 228
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                                59.174 41.075 14.137 1.00 19.84
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            535 CB ARG 228
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            536 CG ARG 228
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            537 CD ARG 228
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            538 NE ARG 228
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            539 CZ ARG 228
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            540 NH1 ARG 228
     ATOM
            541 NH2 ARG 228
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            544 N VAL 229
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            545 CA VAL 229
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            547 CG1 VAL 229
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            549 C VAL 229
            550 O VAL 229
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            552 CA VAL 230
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            555 CG2 VAL 230
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            556 C VAL 230
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            557 O VAL 230
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            560 CB ASP 231
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            562 OD1 ASP 231
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            563 OD2 ASP 231
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            566 N PHE 232
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            567 CA PHE 232
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            572 CE1 PHE 232
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            573 CE2 PHE 232
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    ATOM 574 CZ PHE 232
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            575 C PHE 232
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    ATOM 576 O PHE 232
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            577 N ALA 233
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            578 CA ALA 233
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            588 NZ LYS 234
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            589 C LYS 234
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            590 O LYS 234
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            597 NZ LYS 235
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            603 CG LEU 236
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    ATOM 618 CG MET 238
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    ATOM 620 CE MET 238
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            626 CG PHE 239
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    ATOM 627 CD1 PHE 239
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            629 CE1 PHE 239
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    ATOM 630 CE2 PHE 239
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            645 OE1 GLU 241
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                                45.211 24.679 14.805 1.00 68.60
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            646 OE2 GLU 241
     ATOM
            647 C GLU 241
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                               45.747 28.103 20.498 1.00 34.71
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            650 CA LEU 242
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                               48.345 27.006 22.455 1.00 30.51
            652 CG LEU 242
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                               44.913 29.089 23.938 1.00 32.37
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            662 C PRO 243
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                               46.461 31.110 24.809 1.00 38.79
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            669 C CYS 244
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            670 O CYS 244
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            671 N GLU 245
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                                47.156 32.939 28.337 1.00 34.60
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            673 CB GLU 245
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                                45.356 33.171 30.160 1.00 41.92
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            674 CG GLU 245
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                                 43.080 32.693 30.618 1.00 38.31
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                                 43.697 32.644 28.516 1.00 48.13
            677 OE2 GLU 245
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            679 O GLU 245
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                                47.863 26.742 26.772 1.00 35.79
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            685 OD2 ASP 246
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            686 C ASP 246
                               51.331 30.789 25.863 1.00 27.35
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            690 CB GLN 247
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                                48.303 32.213 22.091 1.00 23.76
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            695 C GLN 247
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            696 O GLN 247
                                52.326 33.373 24.205 1.00 27.63
     ATOM
                               50.588 34.047 25.473 1.00 25.03
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                               51.353 35.035 26.220 1.00 25.94
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                               50.436 35.781 27.226 1.00 24.84
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     ATOM
                                51.251 36.633 28.179 1.00 21.87
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                                49.430 36.652 26.459 1.00 27.98
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                              52.535 34.382 26.939 1.00 27.53
             703 C ILE 248
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                              52.279 33.274 27.622 1.00 24.38
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            706 CA ILE 249
     ATOM
                              52.759 31.395 29.166 1.00 29.81
            707 CB ILE 249
     ATOM
                               53.874 30.521 29.726 1.00 29.16
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            708 CG2 ILE 249
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            710 CD1 ILE 249
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            711 C ILE 249
            712 O ILE 249
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                               54.061 31.516 26.289 1.00 29.25
            713 N LEU 250
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            714 CA LEU 250
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            715 CB LEU 250
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            716 CG LEU 250
     ATOM
                                52.886 28.353 23.416 1.00 19.94
            717 CD1 LEU 250
     ATOM
            718 CD2 LEU 250
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            719 C LEU 250
                               55.878 32.116 24.714 1.00 22.20
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           720 O LEU 250
                               57.082 31.940 24.528 1.00 23.49
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                               55.256 33.249 24.399 1.00 24.21
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            722 CA LEU 251
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           723 CB LEU 251
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     ATOM 724 CG LEU 251
     ATOM 725 CD1 LEU 251
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                                55.268 35.364 20.924 1.00 23.65
     ATOM 726 CD2 LEU 251
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     ATOM 727 C LEU 251
                               58.165 35.143 24.484 1.00 23.12
     ATOM 728 O LEU 251
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     ATOM 730 CA LYS 252
                                56.659 35.723 28.437 1.00 37.06
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            731 CB LYS 252
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     ATOM 732 CG LYS 252
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             733 CD LYS 252
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            734 CE LYS 252
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            735 NZ LYS 252
             736 C LYS 252
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            737 O LYS 252
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            738 N GLY 253
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                                59.407 32.416 27.369 1.00 22.80
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             739 CA GLY 253
                               60.413 32.282 26.235 1.00 26.90
             740 C GLY 253
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            741 O GLY 253
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                               60.013 32.574 24.997 1.00 25.42
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     ATOM
             743 CA CYS 254
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                                60.314 31.509 22.811 1.00 24.98
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             744 CB CYS 254
                                58.976 32.310 21.909 1.00 24.24
             745 SG CYS 254
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                               61.353 33.716 23.164 1.00 22.79
     ATOM
             746 C CYS 254
     ATOM
             747 O CYS 254
                               62.217 33.683 22.282 1.00 23.23
             748 N CYS 255
                               60.757 34.842 23.539 1.00 21.47
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     ATOM
                                61.061 36.114 22.884 1.00 22.50
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     ATOM
             750 CB CYS 255
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                                60.353 38.768 22.597 1.00 24.73
             751 SG CYS 255
     ATOM
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             753 O CYS 255
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            756 CB MET 256
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                                66.781 37.094 25.272 1.00 17.41
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            757 CG MET 256
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            758 SD MET 256
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            764 CB GLU 257
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            768 OE2 GLU 257
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            776 CD1 ILE 258
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     ATOM
            777 C ILE 258
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            778 O ILE 258
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                               64.865 36.410 19.274 1.00 20.17
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                                65.584 37.628 18.909 1.00 15.03
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            780 CA MET 259
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            781 CB MET 259
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            783 SD MET 259
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            784 CE MET 259
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            786 O MET 259
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            790 OG SER 260
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            791 C SER 260
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            793 N LEU 261
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            794 CA LEU 261
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            795 CB LEU 261
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                                67.719 31.759 15.781 1.00 22.12
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            796 CG LEU 261
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             797 CD1 LEU 261
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             798 CD2 LEU 261
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                               68.873 34.527 15.920 1.00 22.95
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                               67.816 36.301 14.643 1.00 25.32
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            803 CB ARG 262
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804 CG ARG 262
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                               62.990 36.377 13.599 1.00 22.18
    ATOM 806 NE ARG 262
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            807 CZ ARG 262
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                                61.429 38.075 13.752 1.00 20.81
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    ATOM 808 NH1 ARG 262
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    ATOM 809 NH2 ARG 262
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    ATOM 810 C ARG 262
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    ATOM 811 O ARG 262
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           812 N ALA 263
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                               70.818 38.400 15.705 1.00 27.02
            813 CA ALA 263
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                              72.026 37.514 15.368 1.00 25.21
     ATOM 815 C ALA 263
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                               73.203 35.408 15.828 1.00 23.85
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            819 CB ALA 264
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                               74.460 34.773 13.886 1.00 25.66
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           823 CA VAL 265
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     ATOM 824 CB VAL 265
     ATOM 825 CG1 VAL 265
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                                69.881 34.440 11.853 1.00 20.86
           826 CG2 VAL 265
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     ATOM 827 C VAL 265
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     ATOM 831 CB ARG 266
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     ATOM 834 NE ARG 266
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     ATOM 836 NH1 ARG 266
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     ATOM 846 CD2 TYR 267
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     ATOM 847 CE2 TYR 267
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                               79.248 38.963 10.133 1.00 45.56
     ATOM 853 CA ASP 268
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           857 OD2 ASP 268
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            881 CG ASP 272
            882 OD1 ASP 272
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            891 C THR 273
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            894 CA LEU 274
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            897 CD1 LEU 274
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            898 CD2 LEU 274
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                              74.943 42.163 14.347 1.00 36.49
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    ATOM
            903 CB THR 275
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            908 N LEU 276
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            911 CG LEU 276
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            912 CD1 LEU 276
    ATOM
    ATOM
            913 CD2 LEU 276
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                              69.175 45.335 13.510 1.00 33.87
    ATOM 915 O LEU 276
            916 N SER 277
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     ATOM
            917 CA SER 277
                               66.721 43.935 13.315 1.00 30.61
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            918 CB SER 277
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            919 OG SER 277
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                              67.103 44.200 11.860 1.00 31.85
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            921 O SER 277
                              66.433 44.958 11.158 1.00 32.13
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                               68.188 43.566 11.421 1.00 32.29
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            922 N GLY 278
            923 CA GLY 278
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     ATOM
                               69.063 45.122 9.639 1.00 43.26
            924 C GLY 278
     ATOM
                               69.313 45.358 8.455 1.00 42.60
            925 O GLY 278
    ATOM
                               69.177 46.038 10.599 1.00 43.42
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                               69.532 47.420 10.291 1.00 44.55
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     ATOM 928 CB GLU 279
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                               67.671 48.344 11.783 1.00 54.19
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     ATOM
            930 CD GLU 279
                               66.400 49.171 11.845 1.00 64.96
     ATOM
            931 OE1 GLU 279
                                65.627 49.174 10.859 1.00 71.43
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            932 OE2 GLU 279
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                               70.654 48.019 11.133 1.00 45.52
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     ATOM
            936 CA MET 280
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     ATOM
            937 CB MET 280
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                                72.479 49.058 15.345 1.00 37.87
            938 CG MET 280
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            939 SD MET 280
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                               70.650 50.495 16.911 1.00 37.01
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     ATOM
                               72.976 45.900 14.044 1.00 36.99
     ATOM
            942 O MET 280
            943 N ALA 281
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            944 CA ALA 281
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            945 CB ALA 281
            946 C ALA 281
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            947 O ALA 281
     ATOM
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            948 N VAL 282
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            949 CA VAL 282
                               76.839 46.246 16.655 1.00 36.05
     ATOM
                               75.783 46.090 17.783 1.00 35.60
            950 CB VAL 282
     ATOM
                               74.633 47.069 17.568 1.00 38.73
     ATOM
            951 CG1 VAL 282
            952 CG2 VAL 282
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     ATOM
                               78.062 45.408 16.996 1.00 37.70
            953 C VAL 282
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78.137 44.223 16.660 1.00 37.45
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                               80.254 45.375 18.048 1.00 43.73
            956 CA ALA 283
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                               81.433 46.352 18.047 1.00 42.04
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    ATOM
            958 C ALA 283
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            959 O ALA 283
                               79.179 45.157 20.203 1.00 45.77
    ATOM
                               80.903 43.774 19.744 1.00 41.96
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    ATOM
                               80.866 43.044 21.004 1.00 44.87
            961 CA ARG 284
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            962 CB ARG 284
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    ATOM
                                81.930 40.947 22.017 1.00 51.85
            963 CG ARG 284
    ATOM
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                                83.107 40.010 21.844 1.00 60.73
            964 CD ARG 284
    ATOM
            965 NE ARG 284
                                83.262 39.571 20.455 1.00 54.30
    ATOM
            966 CZ ARG 284
                                83.221 38.300 20.074 1.00 53.66
    ATOM
                                83.032 37.343 20.973 1.00 49.99
            967 NH1 ARG 284
    ATOM
                                83.379 37.984 18.797 1.00 47.31
            968 NH2 ARG 284
    ATOM
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                               80.803 43.945 22.237 1.00 44.85
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            972 CA GLU 285
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            973 CB GLU 285
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            974 C GLU 285
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            975 O GLU 285
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            978 CB GLN 286
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                                79.324 49.710 18.987 1.00 49.48
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                                79.253 48.856 18.097 1.00 48.41
     ATOM
            981 OE1 GLN 286
            982 NE2 GLN 286
                                79.125 51.000 18.755 1.00 47.15
     ATOM
                               77.563 47.255 22.988 1.00 35.40
            983 C GLN 286
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            984 O GLN 286
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            985 N LEU 287
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            986 CA LEU 287
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            987 CB LEU 287
     ATOM
            988 CG LEU 287
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     ATOM
                                73.263 44.305 22.244 1.00 19.41
     ATOM
            989 CD1 LEU 287
            990 CD2 LEU 287
                                74.325 42.221 21.368 1.00 24.84
     ATOM
                               76.234 44.914 24.406 1.00 34.81
            991 C LEU 287
     ATOM
                               75.265 44.857 25.175 1.00 33.92
            992 O LEU 287
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                               77.476 44.621 24.781 1.00 35.38
     ATOM
            993 N LYS 288
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                               77.814 44.204 26.140 1.00 36.12
     ATOM
            994 CA LYS 288
                                79.296 43.839 26.210 1.00 37.13
            995 CB LYS 288
     ATOM
                                79.762 43.280 27.533 1.00 44.61
     ATOM
             996 CG LYS 288
                                81.256 43.018 27.494 1.00 54.07
     ATOM
             997 CD LYS 288
                               81.757 42.435 28.801 1.00 60.87
            998 CE LYS 288
     ATOM
45
                               81.291 41.041 29.039 1.00 61.53
            999 NZ LYS 288
     ATOM
     ATOM 1000 C LYS 288
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                               76.684 45.206 28.013 1.00 40.68
     ATOM 1001 O LYS 288
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     ATOM 1003 CA ASN 289
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    ATOM 1006 OD1 ASN 289
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    ATOM 1007 ND2 ASN 289
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    ATOM 1008 C ASN 289
    ATOM 1009 O ASN 289
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                               75.883 48.032 26.466 1.00 32.65
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    ATOM 1011 CA GLY 290
    ATOM 1012 C GLY 290
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                               72.362 48.480 27.234 1.00 31.06
    ATOM 1013 O GLY 290
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    ATOM 1014 N GLY 291
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                                72.929 46.413 28.937 1.00 25.24
    ATOM 1015 CA GLY 291
    ATOM 1016 C GLY 291
                               72.872 44.900 28.997 1.00 28.12
    ATOM 1017 O GLY 291
                               72.335 44.345 29.955 1.00 31.16
                               73.406 44.223 27.985 1.00 29.51
    ATOM 1018 N LEU 292
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    ATOM 1019 CA LEU 292
    ATOM 1020 CB LEU 292
                                73.304 42.240 26.531 1.00 28.00
                                71.948 42.355 25.827 1.00 23.68
    ATOM 1021 CG LEU 292
                                72.004 41.626 24.509 1.00 26.12
    ATOM 1022 CD1 LEU 292
    ATOM 1023 CD2 LEU 292
                                70.851 41.764 26.694 1.00 23.36
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     ATOM 1025 O LEU 292
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     ATOM 1027 CA GLY 293
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     ATOM 1028 C GLY 293
    ATOM 1029 O GLY 293
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                               77.392 39.848 29.714 1.00 31.88
    ATOM 1030 N VAL 294
                                77.866 38.561 29.217 1.00 35.77
     ATOM 1031 CA VAL 294
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     ATOM 1032 CB VAL 294
                                 79.462 38.092 31.095 1.00 37.54
    ATOM 1033 CG1 VAL 294
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     ATOM 1034 CG2 VAL 294
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                               76.882 37.879 28.274 1.00 35.89
     ATOM 1035 C VAL 294
     ATOM 1036 O VAL 294
                               77.263 36.960 27.541 1.00 37.99
     ATOM 1037 N VAL 295
                               75.619 38.304 28.305 1.00 34.41
                                74.616 37.728 27.413 1.00 32.98
     ATOM 1038 CA VAL 295
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     ATOM 1039 CB VAL 295
                                73.208 38.298 27.677 1.00 31.25
     ATOM 1040 CG1 VAL 295
                                 72.208 37.706 26.694 1.00 23.54
                                 72.783 37.993 29.101 1.00 23.07
     ATOM 1041 CG2 VAL 295
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     ATOM 1042 C VAL 295
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     ATOM 1043 O VAL 295
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     ATOM 1044 N SER 296
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     ATOM 1045 CA SER 296
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     ATOM 1046 CB SER 296
                                77.368 41.478 23.449 1.00 25.43
     ATOM 1047 OG SER 296
     ATOM 1048 C SER 296
                               77.216 38.748 24.045 1.00 35.86
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                               77.220 38.324 22.886 1.00 39.60
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                               78.135 38.402 24.943 1.00 37.41
     ATOM 1050 N ASP 297
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     ATOM 1051 CA ASP 297
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     ATOM 1052 CB ASP 297
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     ATOM 1053 CG ASP 297
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    ATOM 1055 OD2 ASP 297
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    ATOM 1056 C ASP 297
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    ATOM 1057 O ASP 297
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    ATOM 1059 CA ALA 298
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    ATOM 1060 CB ALA 298
    ATOM 1061 C ALA 298
                               76.377 34.408 23.163 1.00 33.04
                               76.538 33.426 22.426 1.00 32.48
    ATOM 1062 O ALA 298
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    ATOM 1065 CB ILE 299
                               74.138 36.789 21.368 1.00 22.98
    ATOM 1066 CG2 ILE 299
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                               73.091 36.707 22.477 1.00 20.91
    ATOM 1067 CG1 ILE 299
                               72.266 37.951 22.634 1.00 19.86
    ATOM 1068 CD1 ILE 299
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    ATOM 1069 C ILE 299
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    ATOM 1070 O ILE 299
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    ATOM 1072 CA PHE 300
                               78.345 36.562 19.726 1.00 28.06
                                79.386 37.565 20.235 1.00 29.06
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    ATOM 1073 CB PHE 300
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    ATOM 1074 CG PHE 300
    ATOM 1075 CD1 PHE 300
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                                80.017 39.209 18.437 1.00 29.11
    ATOM 1076 CD2 PHE 300
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    ATOM 1077 CE1 PHE 300
    ATOM 1078 CE2 PHE 300
                                79.908 40.450 17.815 1.00 29.07
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    ATOM 1079 CZ PHE 300
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    ATOM 1080 C PHE 300
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                               79.767 33.111 20.470 1.00 34.96
    ATOM 1083 CA GLU 301
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    ATOM 1084 CB GLU 301
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    ATOM 1085 C GLU 301
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     ATOM 1086 O GLU 301
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    ATOM 1087 N LEU 302
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    ATOM 1088 CA LEU 302
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     ATOM 1089 CB LEU 302
     ATOM 1090 CG LEU 302
                                73.992 31.006 19.010 1.00 28.73
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     ATOM 1091 CD1 LEU 302
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     ATOM 1092 CD2 LEU 302
     ATOM 1093 C LEU 302
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     ATOM 1096 CA GLY 303
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     ATOM 1097 C GLY 303
    ATOM 1098 O GLY 303
                               77.889 32.619 14.125 1.00 29.18
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                               79.132 33.182 15.912 1.00 31.15
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     ATOM 1100 CA ALA 304
     ATOM 1101 CB ALA 304
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    ATOM 1103 O ALA 304
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79.753 30.414 15.892 1.00 33.91
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    ATOM 1105 CA SER 305
                               79.395 28.237 16.980 1.00 32.71
    ATOM 1106 CB SER 305
                               78.265 28.749 17.663 1.00 48.66
    ATOM 1107 OG SER 305
                              78.558 28.619 14.641 1.00 37.61
    ATOM 1108 C SER 305
    ATOM 1109 O SER 305
                               78,747 27.697 13.845 1.00 39.92
                               77.443 29.349 14.651 1.00 38.21
    ATOM 1110 N LEU 306
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    ATOM 1111 CA LEU 306
    ATOM 1112 CB LEU 306
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                               74.209 29.374 15.212 1.00 26.18
    ATOM 1113 CG LEU 306
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    ATOM 1115 CD2 LEU 306
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     ATOM 1121 OG SER 307
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     ATOM 1122 C SER 307
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     ATOM 1123 O SER 307
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     ATOM 1125 CA ALA 308
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     ATOM 1126 CB ALA 308
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     ATOM 1127 C ALA 308
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     ATOM 1130 CA PHE 309
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     ATOM 1131 CB PHE 309
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     ATOM 1132 CG PHE 309
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     ATOM 1133 CD1 PHE 309
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                                74.903 23.867 12.922 1.00 38.03
     ATOM 1134 CD2 PHE 309
                                77.237 24.627 14.210 1.00 41.12
     ATOM 1135 CE1 PHE 309
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     ATOM 1136 CE2 PHE 309
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     ATOM 1137 CZ PHE 309
                               75.361 25.934 8.720 1.00 36.31
     ATOM 1138 C PHE 309
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     ATOM 1140 N ASN 310
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     ATOM 1141 CA ASN 310
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     ATOM 1142 CB ASN 310
                                76.980 27.339 5.501 1.00 68.29
     ATOM 1143 CG ASN 310
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                                 77.297 28.527 5.412 1.00 74.62
     ATOM 1144 OD1 ASN 310
     ATOM 1145 ND2 ASN 310
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                               73.430 27.385 7.013 1.00 38.37
     ATOM 1146 C ASN 310
                               72.882 26.735 6.123 1.00 36.70
     ATOM 1147 O ASN 310
                               72.780 27.865 8.062 1.00 35.22
     ATOM 1148 N LEU 311
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     ATOM 1149 CA LEU 311
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     ATOM 1150 CB LEU 311
     ATOM 1151 CG LEU 311
                                71.458 27.306 10.845 1.00 26.76
                                70,792 27.847 12.104 1.00 21.37
     ATOM 1152 CD1 LEU 311
                                71.217 25.813 10.722 1.00 22.95
     ATOM 1153 CD2 LEU 311
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70.601 28.561 7.206 1.00 34.64
    ATOM 1154 C LEU 311
                               71.087 29.625 6.820 1.00 37.70
    ATOM 1155 O LEU 311
                               69.444 28.091 6.752 1.00 29.40
    ATOM 1156 N ASP 312
                               68.634 28.867 5.823 1.00 28.65
    ATOM 1157 CA ASP 312
                               68.302 28.061 4.545 1.00 24.79
    ATOM 1158 CB ASP 312
 5
                               67.459 26.804 4.804 1.00 21.47
     ATOM 1159 CG ASP 312
                                66.994 26.549 5.932 1.00 27.92
     ATOM 1160 OD1 ASP 312
                                67.250 26.057 3.832 1.00 27.53
     ATOM 1161 OD2 ASP 312
                              67.380 29.346 6.557 1.00 25.92
     ATOM 1162 C ASP 312
     ATOM 1163 O ASP 312
                               67.167 28.985 7.717 1.00 26.98
10
                               66.540 30.122 5.878 1.00 21.78
     ATOM 1164 N ASP 313
                               65.315 30.653 6.471 1.00 22.89
     ATOM 1165 CA ASP 313
                               64.517 31.458 5.439 1.00 29.19
     ATOM 1166 CB ASP 313
     ATOM 1167 CG ASP 313
                               65.216 32.739 5.025 1.00 36.82
                                65.985 33.285 5.845 1.00 41.51
     ATOM 1168 OD1 ASP 313
15
                                64.997 33.203 3.883 1.00 44.19
     ATOM 1169 OD2 ASP 313
                               64.421 29.587 7.085 1.00 25.09
     ATOM 1170 C ASP 313
                               63,778 29.829 8.110 1.00 27.60
     ATOM 1171 O ASP 313
                               64.363 28.420 6.449 1.00 20.90
     ATOM 1172 N THR 314
     ATOM 1173 CA THR 314
                              63.538 27.322 6.942 1.00 22.71
20
                                63,408 26,208 5,884 1,00 22,07
     ATOM 1174 CB THR 314
     ATOM 1175 OG1 THR 314
                               62.825 26.746 4.693 1.00 23.15
                                62.542 25.079 6.401 1.00 18.17
     ATOM 1176 CG2 THR 314
     ATOM 1177 C THR 314
                               64.080 26.734 8.249 1.00 19.95
                               63.326 26.477 9.182 1.00 22.40
25
     ATOM 1178 O THR 314
                               65.391 26.536 8.318 1.00 20.01
     ATOM 1179 N GLU 315
                                65.997 25.987 9.523 1.00 19.40
     ATOM 1180 CA GLU 315
                                67.454 25.626 9.254 1.00 11.72
     ATOM 1181 CB GLU 315
                                67.544 24.440 8.322 1.00 13.43
     ATOM 1182 CG GLU 315
                                68.925 24.157 7.791 1.00 18.51
     ATOM 1183 CD GLU 315
30
                                69.666 25.107 7.451 1.00 23.24
     ATOM 1184 OE1 GLU 315
                                69.254 22.962 7.673 1.00 24.23
     ATOM 1185 OE2 GLU 315
                               65.833 26.960 10.681 1.00 20.12
     ATOM 1186 C GLU 315
     ATOM 1187 O GLU 315
                               65.425 26.570 11.777 1.00 20.53
                               66.055 28.240 10.406 1.00 21.79
     ATOM 1188 N VAL 316
35
                                65.898 29.270 11.425 1.00 18.14
     ATOM 1189 CA VAL 316
                                66.346 30.659 10.898 1.00 18.97
     ATOM 1190 CB VAL 316
                                66.040 31.741 11.929 1.00 19.08
     ATOM 1191 CG1 VAL 316
                                67.840 30.641 10.537 1.00 17.97
     ATOM 1192 CG2 VAL 316
                               64.430 29.332 11.880 1.00 22.54
     ATOM 1193 C VAL 316
40
                               64.146 29.433 13.072 1.00 26.47
     ATOM 1194 O VAL 316
                               63.505 29.242 10.924 1.00 19.66
     ATOM 1195 N ALA 317
                                62.076 29.286 11.216 1.00 16.99
     ATOM 1196 CA ALA 317
                                61.279 29.329 9.926 1.00 17.79
     ATOM 1197 CB ALA 317
45
     ATOM 1198 C ALA 317
                               61.619 28.105 12.063 1.00 14.12
     ATOM 1199 O ALA 317
                               60.808 28.263 12.970 1.00 17.04
                               62.104 26.911 11.740 1.00 20.37
     ATOM 1200 N LEU 318
                                61.725 25.714 12.485 1.00 21.12
     ATOM 1201 CA LEU 318
     ATOM 1202 CB LEU 318
                                62.131 24.448 11.718 1.00 21.80
                                61.364 24.265 10.398 1.00 18.11
     ATOM 1203 CG LEU 318
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61.946 23.125 9.594 1.00 16.79
    ATOM 1204 CD1 LEU 318
    ATOM 1205 CD2 LEU 318
                                59.891 24.024 10.676 1.00 12.66
                               62.335 25.752 13.880 1.00 22.03
    ATOM 1206 C LEU 318
                               61.688 25.373 14.858 1.00 21.35
    ATOM 1207 O LEU 318
    ATOM 1208 N LEU 319
                               63.564 26.257 13.964 1.00 20.03
    ATOM 1209 CA LEU 319
                                64.260 26.395 15.236 1.00 20.24
                                65.657 26.960 15.001 1.00 19.07
    ATOM 1210 CB LEU 319
                                66.594 27.108 16.196 1.00 27.61
    ATOM 1211 CG LEU 319
    ATOM 1212 CD1 LEU 319
                                66.518 25.883 17.083 1.00 29.73
    ATOM 1213 CD2 LEU 319
                                68.012 27.326 15.699 1.00 20.98
10
                               63.422 27.334 16.118 1.00 21.16
    ATOM 1214 C LEU 319
    ATOM 1215 O LEU 319
                               63.144 27.032 17.279 1.00 26.65
    ATOM 1216 N GLN 320
                               62.958 28.439 15.539 1.00 20.77
                                62.119 29.390 16.265 1.00 17.87
    ATOM 1217 CA GLN 320
                                61.781 30.594 15.388 1.00 18.74
    ATOM 1218 CB GLN 320
15
                                62.957 31.496 15.111 1.00 21.07
    ATOM 1219 CG GLN 320
    ATOM 1220 CD GLN 320
                                62.637 32.617 14.150 1.00 22.88
                                61.571 32.653 13.528 1.00 26.07
     ATOM 1221 OE1 GLN 320
     ATOM 1222 NE2 GLN 320
                                 63.574 33.537 14.006 1.00 20.11
    ATOM 1223 C GLN 320
                               60.829 28.728 16.730 1.00 19.08
20
                               60.368 28.976 17.844 1.00 23.39
    ATOM 1224 O GLN 320
     ATOM 1225 N ALA 321
                               60.251 27.886 15.876 1.00 22.71
                                59.010 27.187 16.201 1.00 18.86
     ATOM 1226 CA ALA 321
                                58.495 26.422 14.993 1.00 17.22
     ATOM 1227 CB ALA 321
25
     ATOM 1228 C ALA 321
                               59.220 26.235 17.376 1.00 19.85
                               58.362 26.119 18.250 1.00 19.60
     ATOM 1229 O ALA 321
                               60.368 25.561 17.396 1.00 20.25
     ATOM 1230 N VAL 322
                                60.693 24.628 18.469 1.00 21.32
     ATOM 1231 CA VAL 322
     ATOM 1232 CB VAL 322
                                61.956 23.800 18.116 1.00 20.46
     ATOM 1233 CG1 VAL 322
                                 62.418 22.971 19.304 1.00 20.39
30
     ATOM 1234 CG2 VAL 322
                                 61.662 22.890 16.930 1.00 16.83
     ATOM 1235 C VAL 322
                               60.880 25.393 19.785 1.00 20.67
                               60.444 24.941 20.850 1.00 21.28
     ATOM 1236 O VAL 322
                               61.492 26.574 19.701 1.00 21.14
     ATOM 1237 N LEU 323
                                61.722 27.417 20.869 1.00 22.94
     ATOM 1238 CA LEU 323
35
                                62.610 28.608 20.511 1.00 16.12
     ATOM 1239 CB LEU 323
     ATOM 1240 CG LEU 323
                                64.051 28.291 20.115 1.00 22.28
                                64.719 29.532 19.528 1.00 14.87
     ATOM 1241 CD1 LEU 323
                                 64.816 27.750 21.320 1.00 21.55
     ATOM 1242 CD2 LEU 323
                               60.398 27.932 21.410 1.00 22.55
40
     ATOM 1243 C LEU 323
                               60.185 27.986 22.615 1.00 25.21
     ATOM 1244 O LEU 323
     ATOM 1245 N LEU 324
                               59.507 28.300 20.502 1.00 24.15
                                58.200 28.827 20.855 1.00 19.88
     ATOM 1246 CA LEU 324
     ATOM 1247 CB LEU 324
                                57.499 29.384 19.608 1.00 15.20
     ATOM 1248 CG LEU 324
                                56.067 29.908 19.767 1.00 17.21
45
                                 56.021 31.161 20.637 1.00 15.99
     ATOM 1249 CD1 LEU 324
     ATOM 1250 CD2 LEU 324
                                 55.496 30.208 18.395 1.00 20.03
     ATOM 1251 C LEU 324
                               57.311 27.795 21.536 1.00 19.83
                               56.767 28.064 22.609 1.00 24.47
     ATOM 1252 O LEU 324
                                57.197 26.603 20.956 1.00 25.02
50
     ATOM 1253 N MET 325
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56.339 25.563 21.522 1.00 26.72
    ATOM 1254 CA MET 325
    ATOM 1255 CB MET 325
                               55.823 24.644 20.410 1.00 30.03
                              55.129 25.358 19.241 1.00 25.09
    ATOM 1256 CG MET 325
    ATOM 1257 SD MET 325
                               53.714 26.409 19.672 1.00 27.29
                               52.503 25.220 20.084 1.00 20.67
    ATOM 1258 CE MET 325
5
                              56.995 24.736 22.635 1.00 28.94
    ATOM 1259 C MET 325
    ATOM 1260 O MET 325
                              56.881 23.510 22.672 1.00 32.94
    ATOM 1261 N SER 326
                              57.642 25.418 23.569 1.00 29.36
                             58.311 24.759 24.680 1.00 31.62
    ATOM 1262 CA SER 326
    ATOM 1263 CB SER 326
                               59.554 25.559 25.064 1.00 38.13
10
                               60.277 24.949 26.119 1.00 48.99
    ATOM 1264 OG SER 326
    ATOM 1265 C SER 326
                              57.361 24.653 25.871 1.00 33.69
    ATOM 1266 O SER 326
                              56.620 25.594 26.166 1.00 33.66
    ATOM 1267 N THR 327
                              57.356 23,499 26.536 1.00 38.27
    ATOM 1268 CA THR 327 56.497 23.306 27.701 1.00 38.98
15
    ATOM 1269 CB THR 327
                               55.875 21.896 27.730 1.00 33.30
                              56.908 20.911 27.627 1.00 44.01
    ATOM 1270 OG1 THR 327
                              54.888 21.722 26.587 1.00 38.09
    ATOM 1271 CG2 THR 327
    ATOM 1272 C THR 327
                              57.239 23.570 29.018 1.00 42.88
    ATOM 1273 O THR 327
                              56.702 23.325 30.099 1.00 43.36
20
                              58.462 24.091 28.924 1.00 45.92
    ATOM 1274 N ASP 328
    ATOM 1275 CA ASP 328
                               59.268 24.410 30.104 1.00 49.59
    ATOM 1276 CB ASP 328
                               60.760 24.411 29.760 1.00 59.87
    ATOM 1277 CG ASP 328
                               61.273 23.040 29.387 1.00 75.73
                               62.008 22.939 28.382 1.00 85.81
    ATOM 1278 OD1 ASP 328
25
    ATOM 1279 OD2 ASP 328
                               60.946 22.063 30.098 1.00 85.56
                              58.873 25.767 30.673 1.00 48.50
    ATOM 1280 C ASP 328
                              59.725 26.609 30.961 1.00 57.50
    ATOM 1281 O ASP 328
                             57.569 25.980 30.805 1.00 49.62
    ATOM 1282 N ARG 329
    ATOM 1283 CA ARG 329
                              57.032 27.222 31.340 1.00 50.52
30
    ATOM 1284 CB ARG 329
                              56.400 28.080 30.230 1.00 53.57
                              57.376 28.828 29.324 1.00 51.09
    ATOM 1285 CG ARG 329
    ATOM 1286 CD ARG 329
                               57.897 27.951 28.204 1.00 49.73
    ATOM 1287 NE ARG 329
                               58.692 28.699 27.233 1.00 47.44
                               60.005 28.569 27.080 1.00 54.28
35
    ATOM 1288 CZ ARG 329
    ATOM 1289 NH1 ARG 329
                               60.688 27.722 27.839 1.00 58.35
    ATOM 1290 NH2 ARG 329
                              60.631 29.256 26.136 1.00 51.92
    ATOM 1291 C ARG 329
                              55.970 26.870 32.375 1.00 51.90
                              55.378 25.790 32.324 1.00 50.77
    ATOM 1292 O ARG 329
    ATOM 1293 N SER 330
                              55.728 27.784 33.303 1.00 50.56
40
    ATOM 1294 CA SER 330
                             54.744 27.564 34.349 1.00 50.67
    ATOM 1295 CB SER 330
                               55.271 28.108 35.678 1.00 46.64
    ATOM 1296 C SER 330
                              53.404 28.213 34.004 1.00 47.63
    ATOM 1297 O SER 330
                              53.371 29.309 33.440 1.00 48.02
    ATOM 1298 N GLY 331
                              52.314 27.496 34.277 1.00 44.44
45
    ATOM 1299 CA GLY 331
                             50,977 28.023 34.044 1.00 38.77
    ATOM 1300 C GLY 331
                              50.236 27.710 32.756 1.00 41.74
    ATOM 1301 O GLY 331
                              49.147 28.246 32.537 1.00 49.57
    ATOM 1302 N LEU 332 50.783 26.841 31.912 1.00 39.75
    ATOM 1303 CA LEU 332
                             50.123 26.502 30.651 1.00 37.55
50
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ATOM 1304 CB LEU 332
                               51.107 25.829 29.694 1.00 32.36
                               52.268 26.659 29.153 1.00 34.40
    ATOM 1305 CG LEU 332
                                53.207 25.749 28.379 1.00 30.22
    ATOM 1306 CD1 LEU 332
                               51.742 27.786 28.277 1.00 23.33
    ATOM 1307 CD2 LEU 332
                              48.921 25.589 30.834 1.00 36.73
    ATOM 1308 C LEU 332
                              48.987 24.608 31.577 1.00 39.29
    ATOM 1309 O LEU 332
                              47.822 25.925 30.168 1.00 36.07
    ATOM 1310 N LEU 333
    ATOM 1311 CA LEU 333
                              46.615 25.107 30.215 1.00 39.58
    ATOM 1312 CB LEU 333
                              45.384 25.906 29.754 1.00 41.08
                               44.601 26.883 30.644 1.00 47.59
    ATOM 1313 CG LEU 333
10
                              44.268 26.213 31.961 1.00 45.65
    ATOM 1314 CD1 LEU 333
                               45.366 28.171 30.874 1.00 47.42
    ATOM 1315 CD2 LEU 333
                              46.791 23.911 29.278 1.00 40.00
    ATOM 1316 C LEU 333
                              46.690 22.754 29.689 1.00 44.77
    ATOM 1317 O LEU 333
                               47.102 24.213 28.022 1.00 37.70
    ATOM 1318 N CYA 334
15
                              47.265 23.209 26.968 1.00 36.04
    ATOM 1319 CA CYA 334
                               46.815 23.808 25.635 1.00 40.64
    ATOM 1320 CB CYA 334
                               45.280 24.738 25.758 1.00 44.31
    ATOM 1321 SG CYA 334
    ATOM 1322 AS CYA 334
                               43.972 22.946 25.380 1.00 76.30
                               48.668 22.617 26.815 1.00 34.91
    ATOM 1323 C CYA 334
20
    ATOM 1324 O CYA 334
                               49.237 22.615 25.722 1.00 37.63
                               49.189 22.056 27.903 1.00 35.43
    ATOM 1325 N VAL 335
                              50.518 21.452 27.909 1.00 34.27
    ATOM 1326 CA VAL 335
                               50.861 20.868 29.298 1.00 34.21
    ATOM 1327 CB VAL 335
                               52.261 20.258 29.292 1.00 33.66
25
    ATOM 1328 CG1 VAL 335
                                50.755 21.945 30.362 1.00 31.77
    ATOM 1329 CG2 VAL 335
                               50.662 20.349 26.865 1.00 37.14
    ATOM 1330 C VAL 335
                               51.639 20.320 26.114 1.00 37.59
    ATOM 1331 O VAL 335
                              49.683 19.451 26.813 1.00 39.99
    ATOM 1332 N ASP 336
                               49.705 18.339 25.866 1.00 41.64
    ATOM 1333 CA ASP 336
30
                               48.532 17.392 26.146 1.00 54.27
    ATOM 1334 CB ASP 336
    ATOM 1335 CG ASP 336
                               48.596 16.118 25.322 1.00 67.42
                               47.915 16.049 24.274 1.00 70.98
    ATOM 1336 OD1 ASP 336
    ATOM 1337 OD2 ASP 336
                                49.337 15.191 25.717 1.00 76.88
                              49.702 18.762 24.393 1.00 38.31
    ATOM 1338 C ASP 336
35
    ATOM 1339 O ASP 336
                              50.469 18.229 23.586 1.00 37.46
                              48.853 19.729 24.052 1.00 30.23
    ATOM 1340 N LYS 337
                               48.740 20.211 22.676 1.00 29.21
    ATOM 1341 CA LYS 337
    ATOM 1342 CB LYS 337
                               47.561 21.189 22.559 1.00 30.53
                               47.012 21.360 21.162 1.00 51.63
    ATOM 1343 CG LYS 337
40
                               45.636 21.997 21.186 1.00 59.57
    ATOM 1344 CD LYS 337
     ATOM 1345 CE LYS 337
                               45.066 22.115 19.774 1.00 66.05
                               43.673 22.693 19.776 1.00 67.20
    ATOM 1346 NZ LYS 337
                               50.054 20.873 22.249 1.00 28.33
    ATOM 1347 C LYS 337
    ATOM 1348 O LYS 337
                               50.581 20.594 21.170 1.00 26.08
45
                              50.609 21.696 23.141 1.00 26.74
    ATOM 1349 N ILE 338
                             51.873 22.390 22.902 1.00 25.42
     ATOM 1350 CA ILE 338
                               52.177 23.379 24.052 1.00 23.57
     ATOM 1351 CB ILE 338
    ATOM 1352 CG2 ILE 338 53.559 23.991 23.874 1.00 22.59
                              51.105 24.471 24.096 1.00 23.57
    ATOM 1353 CG1 ILE 338
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51.157 25.362 25.333 1.00 24.30
    ATOM 1354 CD1 ILE 338
    ATOM 1355 C ILE 338
                              53.018 21.382 22.768 1.00 29.20
                              53.905 21.537 21.916 1.00 31.59
    ATOM 1356 O ILE 338
                               52.977 20.340 23.595 1.00 34.82
    ATOM 1357 N GLU 339
                                53.980 19.277 23.597 1.00 34.23
    ATOM 1358 CA GLU 339
                                53.639 18.256 24.681 1.00 40.38
    ATOM 1359 CB GLU 339
    ATOM 1360 CG GLU 339
                                54.785 17.354 25.072 1.00 54.98
    ATOM 1361 CD GLU 339
                                55.644 17.964 26.178 1.00 71.26
                                56.766 18.444 25.858 1.00 77.82
    ATOM 1362 OE1 GLU 339
    ATOM 1363 OE2 GLU 339
                                55.170 17.985 27.349 1.00 65.14
10
                               53.972 18.582 22.231 1.00 34.42
    ATOM 1364 C GLU 339
                               55.018 18.431 21.590 1.00 29.41
    ATOM 1365 O GLU 339
    ATOM 1366 N LYS 340
                               52.778 18.189 21.786 1.00 34.13
    ATOM 1367 CA LYS 340
                               52.592 17.513 20.502 1.00 32.05
                               51.121 17.105 20.325 1.00 34.59
    ATOM 1368 CB LYS 340
15
                               53.064 18.390 19.337 1.00 32.56
    ATOM 1369 C LYS 340
     ATOM 1370 O LYS 340
                               53.762 17.913 18.441 1.00 32.93
                               52.725 19.677 19.374 1.00 31.42
     ATOM 1371 N SER 341
     ATOM 1372 CA SER 341
                              53.134 20.621 18.334 1.00 27.79
                               52.559 22.009 18.601 1.00 27.85
     ATOM 1373 CB SER 341
20
                              51.149 21.966 18.579 1.00 47.20
     ATOM 1374 OG SER 341
     ATOM 1375 C SER 341
                               54.647 20.713 18.240 1.00 26.01
     ATOM 1376 O SER 341
                               55.205 20.706 17.139 1.00 27.10
                               55.318 20.794 19.389 1.00 24.25
     ATOM 1377 N GLN 342
                                56.771 20.875 19.392 1.00 27.16
25
     ATOM 1378 CA GLN 342
    ATOM 1379 CB GLN 342
                                57.309 21.089 20.799 1.00 25.60
                                58.768 21.466 20.777 1.00 27.99
     ATOM 1380 CG GLN 342
     ATOM 1381 CD GLN 342
                                59.407 21.429 22.133 1.00 29.58
                                60.123 22.356 22.513 1.00 31.18
     ATOM 1382 OE1 GLN 342
                                59.184 20.345 22.868 1.00 29.17
     ATOM 1383 NE2 GLN 342
30
                               57.377 19.609 18.786 1.00 28.45
     ATOM 1384 C GLN 342
                               58.378 19.675 18.062 1.00 29.79
     ATOM 1385 O GLN 342
                               56.777 18.458 19.078 1.00 26.58
     ATOM 1386 N GLU 343
                                57.251 17.190 18.525 1.00 30.07
     ATOM 1387 CA GLU 343
                                56.462 16.016 19.114 1.00 40.79
     ATOM 1388 CB GLU 343
35
     ATOM 1389 CG GLU 343
                                56.812 15.700 20.568 1.00 61.22
     ATOM 1390 CD GLU 343
                                55.951 14.594 21.166 1.00 71.76
     ATOM 1391 OE1 GLU 343
                                55.472 13.719 20.405 1.00 76.73
     ATOM 1392 OE2 GLU 343
                                55.758 14.601 22.403 1.00 74.09
                               57.097 17.225 17.001 1.00 25.87
     ATOM 1393 C GLU 343
40
     ATOM 1394 O GLU 343
                               58.008 16.842 16.260 1.00 27.26
     ATOM 1395 N ALA 344
                               55.947 17.727 16.550 1.00 23.70
                                55.647 17.853 15.124 1.00 22.16
     ATOM 1396 CA ALA 344
                                54.275 18.489 14.927 1.00 21.18
     ATOM 1397 CB ALA 344
                               56.729 18.694 14.454 1.00 21.24
     ATOM 1398 C ALA 344
45
                               57.303 18.284 13.438 1.00 26.47
     ATOM 1399 O ALA 344
                               57.048 19.840 15.055 1.00 22.48
     ATOM 1400 N TYR 345
     ATOM 1401 CA TYR 345
                               58.073 20.738 14.531 1.00 21.41
     ATOM 1402 CB TYR 345
                                58.085 22.059 15.304 1.00 20.10
                              57.023 23.015 14.830 1.00 15.87
50
     ATOM 1403 CG TYR 345
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56.004 23.434 15.682 1.00 10.54
    ATOM 1404 CD1 TYR 345
                                54.983 24.259 15.225 1.00 17.09
    ATOM 1405 CE1 TYR 345
                                57.003 23.448 13.505 1.00 16.86
    ATOM 1406 CD2 TYR 345
                                55.991 24.269 13.036 1.00 16.84
    ATOM 1407 CE2 TYR 345
                                54.984 24.668 13.896 1.00 17.97
    ATOM 1408 CZ TYR 345
 5
                                53.963 25.455 13.406 1.00 27.11
    ATOM 1409 OH TYR 345
                               59.465 20.120 14.548 1.00 24.43
    ATOM 1410 C TYR 345
                               60.238 20.291 13.597 1.00 24.69
    ATOM 1411 O TYR 345
                               59.777 19.401 15.621 1.00 26.75
    ATOM 1412 N LEU 346
                               61.074 18.746 15.767 1.00 25.06
     ATOM 1413 CA LEU 346
10
                                61.207 18.108 17.150 1.00 24.59
     ATOM 1414 CB LEU 346
                                61.637 19.076 18.252 1.00 26.46
     ATOM 1415 CG LEU 346
                                61.387 18.468 19.610 1.00 26.46
     ATOM 1416 CD1 LEU 346
                                63.101 19.437 18.076 1.00 21.78
     ATOM 1417 CD2 LEU 346
                               61.322 17.713 14.683 1.00 23.24
     ATOM 1418 C LEU 346
15
     ATOM 1419 O LEU 346
                               62.416 17.645 14.127 1.00 27.54
                               60.314 16.900 14.395 1.00 25.75
     ATOM 1420 N LEU 347
                                60.437 15.881 13.356 1.00 25.41
     ATOM 1421 CA LEU 347
                                59.208 14.970 13.330 1.00 23.78
     ATOM 1422 CB LEU 347
                                59.302 13.713 14.190 1.00 31.85
     ATOM 1423 CG LEU 347
20
                                58.004 12.928 14.089 1.00 39.88
     ATOM 1424 CD1 LEU 347
                                60.483 12.864 13.738 1.00 27.65
     ATOM 1425 CD2 LEU 347
                               60.611 16.535 11.998 1.00 23.22
     ATOM 1426 C LEU 347
                               61.468 16.133 11.211 1.00 28.58
     ATOM 1427 O LEU 347
                               59.784 17.542 11.731 1.00 26.40
     ATOM 1428 N ALA 348
25
                                59.840 18.273 10.474 1.00 23.85
     ATOM 1429 CA ALA 348
                                58.732 19.324 10.433 1.00 25.27
     ATOM 1430 CB ALA 348
                               61.210 18.924 10.337 1.00 23.69
     ATOM 1431 C ALA 348
                               61.847 18.835 9.288 1.00 29.11
     ATOM 1432 O ALA 348
                               61.678 19.506 11.438 1.00 24.71
     ATOM 1433 N PHE 349
30
                                62.973 20.181 11.493 1.00 20.48
     ATOM 1434 CA PHE 349
                                63.164 20.772 12.900 1.00 17.84
     ATOM 1435 CB PHE 349
                                64.334 21.721 13.031 1.00 14.90
     ATOM 1436 CG PHE 349
                                65.109 22.069 11.933 1.00 17.58
     ATOM 1437 CD1 PHE 349
                                 64.651 22.269 14.271 1.00 24.77
     ATOM 1438 CD2 PHE 349
35
                                66.185 22.944 12.063 1.00 20.26
     ATOM 1439 CE1 PHE 349
                                65.727 23.147 14.413 1.00 23.83
     ATOM 1440 CE2 PHE 349
                                66.494 23.486 13.299 1.00 20.36
     ATOM 1441 CZ PHE 349
                               64.084 19.181 11.159 1.00 23.43
     ATOM 1442 C PHE 349
                               64.916 19.427 10.278 1.00 24.35
     ATOM 1443 O PHE 349
40
                                64.057 18.028 11.820 1.00 25.79
     ATOM 1444 N GLU 350
                                65.060 16.991 11.606 1.00 26.75
     ATOM 1445 CA GLU 350
                                64.813 15.822 12.567 1.00 29.56
     ATOM 1446 CB GLU 350
                                 65.774 14.661 12.391 1.00 39.94
     ATOM 1447 CG GLU 350
                                 65.574 13.549 13.407 1.00 45.06
     ATOM 1448 CD GLU 350
45
                                 64.413 13.192 13.715 1.00 49.26
     ATOM 1449 OE1 GLU 350
                                 66.593 13.017 13.887 1.00 56.67
     ATOM 1450 OE2 GLU 350
                                65.051 16.494 10.162 1.00 26.95
     ATOM 1451 C GLU 350
                                66.096 16.398 9.513 1.00 28.77
     ATOM 1452 O GLU 350
     ATOM 1453 N HIS 351
                               63.858 16.219 9.652 1.00 22.56
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ATOM 1454 CA HIS 351
                               63.699 15.728 8.294 1.00 22.20
                               62.263 15.265 8.083 1.00 22.47
     ATOM 1455 CB HIS 351
                               61.881 14.106 8.947 1.00 23.61
    ATOM 1456 CG HIS 351
                               62.633 13.300 9.739 1.00 27.65
     ATOM 1457 CD2 HIS 351
                               60.585 13.653 9.069 1.00 26.13
    ATOM 1458 ND1 HIS 351
                               60.548 12.629 9.898 1.00 22.87
     ATOM 1459 CE1 HIS 351
                               61.779 12.393 10.319 1.00 27.53
     ATOM 1460 NE2 HIS 351
                              64.135 16.764 7.259 1.00 21.76
     ATOM 1461 C HIS 351
                              64.708 16.419 6.226 1.00 27.02
     ATOM 1462 O HIS 351
                               63.909 18.041 7.555 1.00 18.26
     ATOM 1463 N TYR 352
10
     ATOM 1464 CA TYR 352
                                64.327 19.101 6.649 1.00 16.94
                                63.749 20.455 7.066 1.00 19.07
     ATOM 1465 CB TYR 352
                                64.107 21.534 6.081 1.00 21.11
     ATOM 1466 CG TYR 352
                                63.518 21.564 4.819 1.00 21.33
     ATOM 1467 CD1 TYR 352
                                63.921 22.482 3.859 1.00 21.06
     ATOM 1468 CE1 TYR 352
15
     ATOM 1469 CD2 TYR 352
                                65.105 22.462 6.367 1.00 22.07
                                65.515 23.388 5.412 1.00 25.40
     ATOM 1470 CE2 TYR 352
     ATOM 1471 CZ TYR 352
                                64.921 23.384 4.161 1.00 21.90
     ATOM 1472 OH TYR 352
                                65.334 24.268 3.197 1.00 23.57
                               65.853 19.156 6.657 1.00 18.49
     ATOM 1473 C TYR 352
20
                               66.487 19.323 5.609 1.00 24.99
     ATOM 1474 O TYR 352
     ATOM 1475 N VAL 353
                               66.451 19.008 7.836 1.00 24.64
                                67.904 19.011 7.955 1.00 22.20
     ATOM 1476 CA VAL 353
                                68.350 18.925 9.440 1.00 23.72
     ATOM 1477 CB VAL 353
                                69.838 18.597 9.546 1.00 21.24
     ATOM 1478 CG1 VAL 353
25
                                68.063 20.245 10.142 1.00 20.07
     ATOM 1479 CG2 VAL 353
                               68.452 17.829 7.146 1.00 25.07
     ATOM 1480 C VAL 353
                               69.467 17.955 6.457 1.00 24.75
     ATOM 1481 O VAL 353
                               67.768 16.690 7.221 1.00 24.59
     ATOM 1482 N ASN 354
                                68.171 15.502 6.474 1.00 25.64
     ATOM 1483 CA ASN 354
30
     ATOM 1484 CB ASN 354
                                67.223 14.331 6.751 1.00 26.05
                                67.368 13.763 8.151 1.00 30.27
     ATOM 1485 CG ASN 354
                                66.443 13.139 8.672 1.00 33.71
     ATOM 1486 OD1 ASN 354
                                 68.529 13.959 8.765 1.00 34.78
     ATOM 1487 ND2 ASN 354
                               68.143 15.813 4.981 1.00 30.50
     ATOM 1488 C ASN 354
35
                               69.042 15.423 4.233 1.00 33.73
     ATOM 1489 O ASN 354
                               67.098 16.519 4.555 1.00 30.54
     ATOM 1490 N HIS 355
                               66.926 16.901 3.157 1.00 26.02
     ATOM 1491 CA HIS 355
     ATOM 1492 CB HIS 355
                               65.535 17.521 2.953 1.00 29.93
     ATOM 1493 CG HIS 355
                               65.367 18.217 1.638 1.00 37.91
40
                                65.654 19.486 1.264 1.00 31.26
     ATOM 1494 CD2 HIS 355
                                64.861 17.593 0.518 1.00 32.67
     ATOM 1495 ND1 HIS 355
     ATOM 1496 CE1 HIS 355
                                64.843 18.447 -0.488 1.00 33.22
     ATOM 1497 NE2 HIS 355
                                65.322 19.601 -0.061 1.00 32.69
                              68.009 17.851 2.652 1.00 24.29
     ATOM 1498 C HIS 355
45
                               68.381 17.798 1.484 1.00 26.82
     ATOM 1499 O HIS 355
     ATOM 1500 N ARG 356
                               68.484 18.735 3.526 1.00 29.72
                                69.516 19.711 3.167 1.00 26.65
     ATOM 1501 CA ARG 356
                                69.593 20.804 4.225 1.00 22.74
     ATOM 1502 CB ARG 356
     ATOM 1503 CG ARG 356
                                68.409 21.735 4.222 1.00 21.64
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68.757 23.024 3.524 1.00 28.04
    ATOM 1504 CD ARG 356
                                69.550 23.900 4.380 1.00 33.79
     ATOM 1505 NE ARG 356
                                70.508 24.716 3.952 1.00 29.26
    ATOM 1506 CZ ARG 356
                                70.814 24.776 2.667 1.00 29.08
    ATOM 1507 NH1 ARG 356
                                71.136 25.493 4.816 1.00 33.61
    ATOM 1508 NH2 ARG 356
    ATOM 1509 C ARG 356
                               70.904 19.115 2.950 1.00 27.58
                               71.757 19.740 2.312 1.00 31.44
    ATOM 1510 O ARG 356
                               71.140 17.937 3.519 1.00 30.56
    ATOM 1511 N LYS 357
    ATOM 1512 CA LYS 357
                               72.422 17.244 3.390 1.00 34.56
                               72.500 16.518 2.043 1.00 39.66
    ATOM 1513 CB LYS 357
10
                               71.476 15.402 1.871 1.00 42.16
    ATOM 1514 CG LYS 357
                               71.674 14.676 0.550 1.00 54.23
    ATOM 1515 CD LYS 357
    ATOM 1516 CE LYS 357
                               70.691 13.523 0.371 1.00 61.97
                               69.288 13.974 0.162 1.00 65.88
    ATOM 1517 NZ LYS 357
                               73.665 18.119 3.606 1.00 36.73
    ATOM 1518 C LYS 357
15
                               74.522 18.248 2.728 1.00 40.70
    ATOM 1519 O LYS 357
                              73.738 18.732 4.786 1.00 33.69
    ATOM 1520 N HIS 358
                               74.863 19.581 5.163 1.00 33.59
     ATOM 1521 CA HIS 358
     ATOM 1522 CB HIS 358
                               74.660 20.155 6.571 1.00 32.07
                               73.593 21.200 6.666 1.00 29.74
    ATOM 1523 CG HIS 358
20
    ATOM 1524 CD2 HIS 358
                               72.245 21.098 6.736 1.00 23.35
                               73.876 22.547 6.731 1.00 28.13
     ATOM 1525 ND1 HIS 358
                               72,752 23,231 6.834 1.00 26.94
     ATOM 1526 CE1 HIS 358
                               71.747 22.373 6.838 1.00 23.32
     ATOM 1527 NE2 HIS 358
25
     ATOM 1528 C HIS 358
                              76.121 18.720 5.180 1.00 37.98
                              76.087 17.581 5.654 1.00 41.07
     ATOM 1529 O HIS 358
                               77.231 19.261 4.690 1.00 44.20
     ATOM 1530 N ASN 359
                                78.492 18.523 4.676 1.00 49.72
     ATOM 1531 CA ASN 359
                                79.406 19.053 3.572 1.00 46.66
     ATOM 1532 CB ASN 359
                               79.174 18.648 6.039 1.00 51.77
     ATOM 1533 C ASN 359
30
                               80.356 18.985 6.122 1.00 57.32
     ATOM 1534 O ASN 359
     ATOM 1535 N ILE 360
                              78.414 18.383 7.101 1.00 51.04
                               78.906 18.471 8.477 1.00 48.24
     ATOM 1536 CA ILE 360
                               78.340 19.721 9.207 1.00 47.20
     ATOM 1537 CB ILE 360
                               78.781 19.741 10.673 1.00 43.50
     ATOM 1538 CG2 ILE 360
35
                               78.777 21.005 8.491 1.00 45.94
     ATOM 1539 CG1 ILE 360
                               78.157 22.262 9.050 1.00 43.00
     ATOM 1540 CD1 ILE 360
                              78,462 17.222 9.239 1.00 47.23
     ATOM 1541 C ILE 360
                              77.272 16.901 9.278 1.00 45.13
     ATOM 1542 O ILE 360
                               79.416 16.490 9.838 1.00 48.61
40
     ATOM 1543 N PRO 361
                                80.869 16.705 9.729 1.00 50.93
     ATOM 1544 CD PRO 361
                                79.129 15.270 10.599 1.00 45.46
     ATOM 1545 CA PRO 361
                                80.524 14.725 10.927 1.00 49.01
     ATOM 1546 CB PRO 361
                                81.402 15.307 9.862 1.00 54.41
     ATOM 1547 CG PRO 361
                               78.330 15.514 11.879 1.00 36.54
     ATOM 1548 C PRO 361
45
                               78.666 16.394 12.672 1.00 39.83
     ATOM 1549 O PRO 361
     ATOM 1550 N HIS 362
                              77.282 14.716 12.075 1.00 31.35
                               76.430 14.798 13.264 1.00 33.34
     ATOM 1551 CA HIS 362
                               77.246 14.495 14.524 1.00 33.77
     ATOM 1552 CB HIS 362
                               78.129 13.292 14.397 1.00 34.40
     ATOM 1553 CG HIS 362
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ATOM 1554 CD2 HIS 362
                                77.837 11.999 14.130 1.00 32.60
                                79.501 13.362 14.506 1.00 36.14
     ATOM 1555 ND1 HIS 362
                                80.017 12.160 14.311 1.00 36.26
    ATOM 1556 CE1 HIS 362
                                79.029 11.316 14.080 1.00 35.73
     ATOM 1557 NE2 HIS 362
    ATOM 1558 C HIS 362
                               75.778 16.164 13.389 1.00 33.55
                               75.539 16.652 14.495 1.00 31.93
    ATOM 1559 O HIS 362
                               75.449 16.748 12.240 1.00 35.83
     ATOM 1560 N PHE 363
                                74.834 18.067 12.166 1.00 30.93
    ATOM 1561 CA PHE 363
    ATOM 1562 CB PHE 363
                                74.464 18.394 10.712 1.00 28.82
                                73.959 19.797 10.514 1.00 26.59
     ATOM 1563 CG PHE 363
10
                                74.846 20.843 10.301 1.00 26.96
     ATOM 1564 CD1 PHE 363
    ATOM 1565 CD2 PHE 363
                                72.596 20.076 10.575 1.00 27.51
                                74.384 22.151 10.155 1.00 31.83
     ATOM 1566 CE1 PHE 363
                                72.124 21.378 10.433 1.00 26.65
     ATOM 1567 CE2 PHE 363
                                73.019 22.417 10.223 1.00 24.42
     ATOM 1568 CZ PHE 363
15
                               73.613 18.235 13.063 1.00 28.73
     ATOM 1569 C PHE 363
                               73.550 19.174 13.848 1.00 25.33
     ATOM 1570 O PHE 363
     ATOM 1571 N TRP 364
                               72.663 17.310 12.969 1.00 22.89
                                71.443 17.405 13.760 1.00 24.19
     ATOM 1572 CA TRP 364
                                70.481 16.254 13.439 1.00 26.31
20
     ATOM 1573 CB TRP 364
                                69.198 16.275 14.228 1.00 20.24
     ATOM 1574 CG TRP 364
                                68.213 17.325 14.262 1.00 24.50
     ATOM 1575 CD2 TRP 364
                                67.175 16.894 15.120 1.00 25.84
     ATOM 1576 CE2 TRP 364
     ATOM 1577 CE3 TRP 364
                                68.106 18.583 13.652 1.00 25.83
                                 68.731 15.289 15.040 1.00 23.61
25
     ATOM 1578 CD1 TRP 364
                                67.515 15.648 15.579 1.00 32.26
     ATOM 1579 NE1 TRP 364
                                66.048 17.674 15.386 1.00 21.95
     ATOM 1580 CZ2 TRP
                          364
     ATOM 1581 CZ3 TRP 364
                                66.979 19.360 13.919 1.00 20.73
                                 65.967 18.899 14.779 1.00 22.37
     ATOM 1582 CH2 TRP 364
                               71.663 17.551 15.267 1.00 28.84
     ATOM 1583 C TRP 364
30
     ATOM 1584 O TRP 364
                               71.246 18.554 15.839 1.00 31.25
                               72.305 16.568 15.932 1.00 29.69
     ATOM 1585 N PRO 365
                                72.790 15.245 15.497 1.00 30.89
     ATOM 1586 CD PRO 365
                                72.499 16.748 17.373 1.00 25.62
     ATOM 1587 CA PRO 365
     ATOM 1588 CB PRO 365
                                73.195 15.451 17.810 1.00 25.50
35
                                73.804 14.915 16.560 1.00 34.15
     ATOM 1589 CG PRO 365
     ATOM 1590 C PRO 365
                               73.320 18.002 17.698 1.00 24.07
                                73.079 18.654 18.711 1.00 23.58
     ATOM 1591 O PRO 365
                                74.250 18.365 16.820 1.00 24.09
     ATOM 1592 N LYS 366
     ATOM 1593 CA LYS 366
                                75.063 19.562 17.027 1.00 29.44
40
     ATOM 1594 CB LYS 366
                                76.131 19.681 15.945 1.00 27.18
                                77.341 18.802 16.149 1.00 23.71
     ATOM 1595 CG LYS 366
     ATOM 1596 CD LYS 366
                                78.304 19.019 15.001 1.00 27.50
     ATOM 1597 CE LYS 366
                                79.624 18.329 15.231 1.00 35.88
                                80.550 18.591 14.097 1.00 41.92
     ATOM 1598 NZ LYS 366
45
                               74.195 20.820 17.012 1.00 32.76
     ATOM 1599 C LYS 366
                                74.326 21.694 17.873 1.00 36.13
     ATOM 1600 O LYS 366
                                73.307 20.907 16.028 1.00 33.70
     ATOM 1601 N LEU 367
                                72.409 22.041 15.905 1.00 30.60
     ATOM 1602 CA LEU 367
                                71.636 21.955 14.587 1.00 24.26
     ATOM 1603 CB LEU 367
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70.675 23.103 14.274 1.00 32.42
    ATOM 1604 CG LEU 367
                                71.394 24.440 14.404 1.00 24.78
     ATOM 1605 CD1 LEU 367
    ATOM 1606 CD2 LEU 367
                                70.098 22.924 12.878 1.00 28.84
                               71.450 22.015 17.087 1.00 31.90
     ATOM 1607 C LEU 367
                               71.113 23.052 17.655 1.00 39.20
     ATOM 1608 O LEU 367
     ATOM 1609 N LEU 368
                               71.051 20.812 17.485 1.00 33.86
                                70.144 20.617 18.608 1.00 32.97
    ATOM 1610 CA LEU 368
                                69.866 19.123 18.759 1.00 34.22
     ATOM 1611 CB LEU 368
    ATOM 1612 CG LEU 368
                                68.458 18.633 19.084 1.00 38.15
                                67.400 19.449 18.345 1.00 27.75
     ATOM 1613 CD1 LEU 368
10
                                68.374 17.154 18.733 1.00 31.51
     ATOM 1614 CD2 LEU 368
     ATOM 1615 C LEU 368
                               70.793 21.181 19.875 1.00 35.29
                               70.128 21.806 20.703 1.00 36.16
     ATOM 1616 O LEU 368
                               72.106 21.001 19.994 1.00 41.13
     ATOM 1617 N MET 369
                                72.857 21.504 21.139 1.00 40.92
     ATOM 1618 CA MET 369
15
                                74.283 20.955 21.115 1.00 43.32
     ATOM 1619 CB MET 369
                                74.383 19.497 21.545 1.00 50.01
     ATOM 1620 CG MET 369
                                75.997 18.770 21.190 1.00 56.63
     ATOM 1621 SD MET 369
     ATOM 1622 CE MET 369
                                77.032 19.596 22.409 1.00 62.26
                               72.872 23.032 21.186 1.00 43.46
     ATOM 1623 C MET 369
20
                               73.137 23.619 22.233 1.00 47.51
     ATOM 1624 O MET 369
                               72.594 23.673 20.053 1.00 41.60
     ATOM 1625 N LYS 370
                                72.561 25.131 19.988 1.00 34.48
     ATOM 1626 CA LYS 370
                                72.689 25.623 18.546 1.00 31.53
     ATOM 1627 CB LYS 370
                                74.012 25.278 17.896 1.00 30.76
25
     ATOM 1628 CG LYS 370
     ATOM 1629 CD LYS 370
                                75.168 25.774 18.731 1.00 32.16
                                76.488 25.388 18.116 1.00 31.08
     ATOM 1630 CE LYS 370
                                77.604 25.822 18.993 1.00 51.52
     ATOM 1631 NZ LYS 370
     ATOM 1632 C LYS 370
                               71.269 25.652 20.606 1.00 36.35
                               71.197 26.806 21.032 1.00 39.02
     ATOM 1633 O LYS 370
30
     ATOM 1634 N VAL 371
                               70.248 24.804 20.652 1.00 34.33
     ATOM 1635 CA VAL 371
                                68.975 25.186 21.249 1.00 36.27
     ATOM 1636 CB VAL 371
                                67.885 24.097 21.046 1.00 36.15
                                 66.600 24.487 21.758 1.00 32.69
     ATOM 1637 CG1 VAL 371
                                 67.612 23.892 19.567 1.00 33.75
     ATOM 1638 CG2 VAL 371
35
                               69.196 25.423 22.745 1.00 41.55
     ATOM 1639 C VAL 371
     ATOM 1640 O VAL 371
                                68.638 26.367 23.316 1.00 40.82
                               70.018 24.581 23.378 1.00 40.42
     ATOM 1641 N THR 372
                                70.300 24.733 24.804 1.00 41.69
     ATOM 1642 CA THR 372
                                71.037 23.499 25.397 1.00 42.36
     ATOM 1643 CB THR 372
40
                                 72.125 23.133 24.548 1.00 53.57
     ATOM 1644 OG1 THR 372
                                 70.090 22.313 25.523 1.00 43.54
     ATOM 1645 CG2 THR 372
                               71.090 26.021 25.048 1.00 38.75
     ATOM 1646 C THR 372
                               70.858 26.714 26.042 1.00 37.51
     ATOM 1647 O THR 372
     ATOM 1648 N ASP 373
                               71.987 26.360 24.122 1.00 36.73
45
                                72.768 27.594 24.223 1.00 30.96
     ATOM 1649 CA ASP 373
                                73.741 27.732 23.047 1.00 31.26
     ATOM 1650 CB ASP 373
     ATOM 1651 CG ASP 373
                                74.865 26.707 23.085 1.00 35.85
                                75.523 26.508 22.042 1.00 36.73
     ATOM 1652 OD1 ASP 373
                                75.102 26.103 24.153 1.00 39.92
50
     ATOM 1653 OD2 ASP 373
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ATOM 1654 C ASP 373
                               71.797 28.769 24.230 1.00 31.30
                               71.926 29.689 25.039 1.00 35.37
     ATOM 1655 O ASP 373
     ATOM 1656 N LEU 374
                               70.804 28.711 23.348 1.00 27.72
                                69.783 29.751 23.257 1.00 28.18
     ATOM 1657 CA LEU 374
                                68.881 29.521 22.042 1.00 28.41
     ATOM 1658 CB LEU 374
 5
     ATOM 1659 CG LEU 374
                                69.391 30.055 20.703 1.00 29.87
                                68.533 29.520 19.563 1.00 25.44
     ATOM 1660 CD1 LEU 374
     ATOM 1661 CD2 LEU 374
                                69.385 31.581 20.728 1.00 23.74
     ATOM 1662 C LEU 374
                               68.946 29.786 24.527 1.00 28.61
                               68.516 30.859 24.968 1.00 29.51
10
     ATOM 1663 O LEU 374
     ATOM 1664 N ARG 375
                               68.690 28.615 25.105 1.00 32.32
                                67.925 28.532 26.345 1.00 33.19
     ATOM 1665 CA ARG 375
                                67.758 27.074 26.776 1.00 41.70
     ATOM 1666 CB ARG 375
     ATOM 1667 CG ARG 375
                                66.360 26.524 26.609 1.00 51.03
     ATOM 1668 CD ARG 375
                                65.979 26.416 25.153 1.00 60.16
15
     ATOM 1669 NE ARG 375
                                64.648 25.840 24.987 1.00 74.28
     ATOM 1670 CZ ARG 375
                                64.324 24.587 25.296 1.00 79.34
                                65.233 23.756 25.796 1.00 80.84
     ATOM 1671 NH1 ARG 375
     ATOM 1672 NH2 ARG 375
                                 63.084 24.157 25.092 1.00 77.44
                               68.692 29.296 27.423 1.00 32.02
20
     ATOM 1673 C ARG 375
     ATOM 1674 O ARG 375
                               68.132 30.150 28.108 1.00 30.42
                               69.993 29.020 27.521 1.00 32.30
     ATOM 1675 N MET 376
     ATOM 1676 CA MET 376
                                70.860 29.668 28.499 1.00 36.82
                                72.278 29.097 28.433 1.00 45.36
     ATOM 1677 CB MET 376
                                72.375 27.645 28.866 1.00 66.71
25
     ATOM 1678 CG MET 376
     ATOM 1679 SD MET 376
                                74.078 27.057 28.966 1.00 89.64
                                74.256 26.229 27.400 1.00 85.51
     ATOM 1680 CE MET 376
                               70.880 31.182 28.310 1.00 37.49
     ATOM 1681 C MET 376
                               70.780 31.928 29.281 1.00 39.99
     ATOM 1682 O MET 376
                              71.008 31.630 27.060 1.00 33.14
     ATOM 1683 N ILE 377
30
     ATOM 1684 CA ILE 377
                               71.009 33.057 26.740 1.00 25.98
     ATOM 1685 CB ILE 377
                               71.181 33.291 25.211 1.00 22.79
     ATOM 1686 CG2 ILE 377
                               70.838 34.727 24.834 1.00 25.29
     ATOM 1687 CG1 ILE 377
                                72.606 32.947 24.785 1.00 21.42
                                72.816 32.971 23.282 1.00 19.37
35
     ATOM 1688 CD1 ILE 377
                              69.690 33.664 27.228 1.00 27.11
     ATOM 1689 C ILE 377
                              69.676 34.727 27.856 1.00 28.09
     ATOM 1690 O ILE 377
                               68.584 32.969 26.975 1.00 29.34
     ATOM 1691 N GLY 378
     ATOM 1692 CA GLY 378
                                67.292 33.457 27.418 1.00 30.41
                               67.233 33.532 28.934 1.00 36.85
     ATOM 1693 C GLY 378
40
     ATOM 1694 O GLY 378
                               66.672 34.481 29.489 1.00 36.44
     ATOM 1695 N ALA 379
                               67.837 32.547 29.603 1.00 37.98
     ATOM 1696 CA ALA 379
                                67.869 32.483 31.066 1.00 36.44
     ATOM 1697 CB ALA 379
                                68.415 31.133 31.528 1.00 35.63
45
     ATOM 1698 C ALA 379
                               68.712 33.613 31.642 1.00 34.14
                               68.259 34.343 32.523 1.00 35.15
     ATOM 1699 O ALA 379
                               69.941 33.747 31.144 1.00 36.66
     ATOM 1700 N CYA 380
     ATOM 1701 CA CYA 380
                               70.860 34.795 31.587 1.00 37.27
                                72.172 34.728 30.810 1.00 36.85
     ATOM 1702 CB CYA 380
                                73.201 33.338 31.250 1.00 52.80
50
     ATOM 1703 SG CYA 380
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ATOM 1704 AS CYA 380
                               74.942 33.593 29.823 1.00 65.79
                               70.230 36.165 31.398 1.00 38.70
    ATOM 1705 C CYA 380
                               70.337 37.033 32.270 1.00 45.73
    ATOM 1706 O CYA 380
                              69.555 36.354 30.265 1.00 37.32
    ATOM 1707 N HIS 381
                               68.906 37.623 29.994 1.00 32.11
    ATOM 1708 CA HIS 381
5
                               68.377 37.687 28.565 1.00 25.76
    ATOM 1709 CB HIS 381
                               67.596 38.932 28.285 1.00 20.30
    ATOM 1710 CG HIS 381
                               67.998 40.200 28.044 1.00 16.31
    ATOM 1711 CD2 HIS 381
                               66.218 38.971 28.336 1.00 22.06
    ATOM 1712 ND1 HIS 381
                               65.807 40.210 28.146 1.00 21.20
    ATOM 1713 CE1 HIS 381
10
                               66.869 40.976 27.968 1.00 22.58
    ATOM 1714 NE2 HIS 381
                              67.773 37.893 30.980 1.00 32.68
    ATOM 1715 C HIS 381
                              67.602 39.024 31.431 1.00 33.38
    ATOM 1716 O HIS 381
                               66.982 36.873 31.296 1.00 31.27
    ATOM 1717 N ALA 382
                                65.884 37.045 32.243 1.00 29.39
    ATOM 1718 CA ALA 382
15
                                65.121 35.742 32.409 1.00 25.18
    ATOM 1719 CB ALA 382
                               66.420 37.531 33.596 1.00 34.32
    ATOM 1720 C ALA 382
                               65.902 38.501 34.160 1.00 37.79
    ATOM 1721 O ALA 382
                               67.483 36.893 34.085 1.00 36.88
    ATOM 1722 N SER 383
                               68.100 37.268 35.361 1.00 39.74
    ATOM 1723 CA SER 383
20
    ATOM 1724 CB SER 383
                               69.233 36.297 35.719 1.00 42.58
                                68.734 35.010 36.049 1.00 61.85
    ATOM 1725 OG SER 383
                               68.638 38.697 35.311 1.00 36.49
    ATOM 1726 C SER 383
    ATOM 1727 O SER 383
                               68.443 39.480 36.243 1.00 43.81
                               69.305 39.036 34.213 1.00 33.66
25
    ATOM 1728 N ARG 384
                               69.866 40.367 34.043 1.00 35.39
    ATOM 1729 CA ARG 384
                                70.800 40.404 32.835 1.00 29.29
    ATOM 1730 CB ARG 384
                                71.590 41.679 32.731 1.00 29.20
    ATOM 1731 CG ARG 384
                                72.881 41.435 31.995 1.00 37.73
    ATOM 1732 CD ARG 384
                                73.657 42.663 31.850 1.00 48.97
    ATOM 1733 NE ARG 384
30
                                74.346 43.245 32.826 1.00 45.41
    ATOM 1734 CZ ARG 384
                                74.371 42.715 34.038 1.00 44.51
    ATOM 1735 NH1 ARG 384
                                 75.008 44.368 32.584 1.00 41.43
    ATOM 1736 NH2 ARG 384
                               68.777 41.431 33.916 1.00 39.45
    ATOM 1737 C ARG 384
                               68.913 42.537 34.444 1.00 44.47
35
    ATOM 1738 O ARG 384
    ATOM 1739 N PHE 385
                               67,673 41.077 33.270 1.00 36.42
                                66.568 42.007 33.099 1.00 34.68
    ATOM 1740 CA PHE 385
                                65.444 41.393 32.262 1.00 30.21
    ATOM 1741 CB PHE 385
                                64.263 42.304 32.081 1.00 29.48
     ATOM 1742 CG PHE 385
    ATOM 1743 CD1 PHE 385
                                64.289 43.313 31.127 1.00 29.70
40
                                63.130 42.161 32.873 1.00 28.04
     ATOM 1744 CD2 PHE 385
     ATOM 1745 CE1 PHE 385
                                63.203 44.169 30.966 1.00 33.50
                                62.040 43.012 32.718 1.00 31.35
     ATOM 1746 CE2 PHE 385
     ATOM 1747 CZ PHE 385
                                62.077 44.017 31.763 1.00 32.08
                               66.040 42.412 34.468 1.00 35.76
     ATOM 1748 C PHE 385
45
                               65.761 43.590 34.693 1.00 40.58
     ATOM 1749 O PHE 385
     ATOM 1750 N LEU 386
                               65.906 41.441 35.373 1.00 37.55
                               65.429 41.706 36.735 1.00 41.01
     ATOM 1751 CA LEU 386
                                65.394 40.413 37.563 1.00 42.30
     ATOM 1752 CB LEU 386
                                64.240 39.434 37.317 1.00 43.34
     ATOM 1753 CG LEU 386
50
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ATOM 1754 CD1 LEU 386
                               64.559 38.066 37.912 1.00 43.50
                                62,946 39,992 37.899 1.00 44.01
    ATOM 1755 CD2 LEU 386
                               66.342 42.735 37.405 1.00 40.08
    ATOM 1756 C LEU 386
                               65.875 43.632 38.112 1.00 42.08
    ATOM 1757 O LEU 386
                              67.643 42.613 37.153 1.00 34.86
    ATOM 1758 N HIS 387
 5
    ATOM 1759 CA HIS 387
                               68.631 43.537 37.700 1.00 39.09
                               70.046 43.034 37.421 1.00 39.99
    ATOM 1760 CB HIS 387
                               70.402 41.791 38.172 1.00 56.37
    ATOM 1761 CG HIS 387
    ATOM 1762 CD2 HIS 387
                               71.384 40.881 37.974 1.00 60.11
                               69.711 41.370 39.290 1.00 60.40
    ATOM 1763 ND1 HIS 387
10
                               70.252 40.255 39.746 1.00 61.89
    ATOM 1764 CE1 HIS 387
                               71.269 39.937 38.966 1.00 63.96
    ATOM 1765 NE2 HIS 387
                              68.446 44.928 37.101 1.00 41.00
    ATOM 1766 C HIS 387
    ATOM 1767 O HIS 387
                              68.492 45.927 37.817 1.00 46.99
                               68.213 44.982 35.792 1.00 39.15
    ATOM 1768 N MET 388
15
    ATOM 1769 CA MET 388
                                68.011 46.243 35.088 1.00 35.32
                                67.676 45.992 33.612 1.00 35.12
    ATOM 1770 CB MET 388
    ATOM 1771 CG MET 388
                                68.810 45.442 32.753 1.00 37.24
                                68.259 45.150 31.051 1.00 41.75
    ATOM 1772 SD MET 388
                                69.274 43.748 30.573 1.00 35.23
    ATOM 1773 CE MET 388
20
                               66.880 47.048 35.733 1.00 36.52
    ATOM 1774 C MET 388
    ATOM 1775 O MET 388
                               66.994 48.265 35.888 1.00 43.39
    ATOM 1776 N LYS 389
                               65.792 46.371 36.103 1.00 38.05
                               64.637 47.025 36.729 1.00 42.88
    ATOM 1777 CA LYS 389
    ATOM 1778 CB LYS 389
                                63.481 46.035 36.866 1.00 47.83
25
                                62.835 45.627 35.560 1.00 52.36
    ATOM 1779 CG LYS 389
                                62.040 44.340 35.731 1.00 61.84
    ATOM 1780 CD LYS 389
                               60.978 44.451 36.814 1.00 69.04
    ATOM 1781 CE LYS 389
                                60.254 43.162 36.987 1.00 70.00
    ATOM 1782 NZ LYS 389
                               64.983 47.587 38.107 1.00 43.99
    ATOM 1783 C LYS 389
30
    ATOM 1784 O LYS 389
                               64.455 48.621 38.525 1.00 44.22
                               65.851 46.878 38.816 1.00 45.50
    ATOM 1785 N VAL 390
                                66.290 47.286 40.142 1.00 47.76
    ATOM 1786 CA VAL 390
                                67.152 46.186 40.804 1.00 46.30
    ATOM 1787 CB VAL 390
                                67.796 46.706 42.079 1.00 49.20
    ATOM 1788 CG1 VAL 390
35
                                66.305 44.962 41.097 1.00 42.69
    ATOM 1789 CG2 VAL 390
                               67.109 48.571 40.070 1.00 47.25
    ATOM 1790 C VAL 390
    ATOM 1791 O VAL 390
                               66.811 49.540 40.760 1.00 48.67
                               68.115 48.580 39.199 1.00 44.11
     ATOM 1792 N GLU 391
                                69.009 49.721 39.047 1.00 45.79
    ATOM 1793 CA GLU 391
40
    ATOM 1794 CB GLU 391
                                70.266 49.311 38.273 1.00 45.78
                                70.998 48.091 38.830 1.00 57.29
     ATOM 1795 CG GLU 391
     ATOM 1796 CD GLU 391
                                71.479 48.268 40.261 1.00 61.20
    ATOM 1797 OE1 GLU 391
                                71.845 49.400 40.646 1.00 57.29
                                71.496 47.263 41.001 1.00 63.69
    ATOM 1798 OE2 GLU 391
45
                               68.410 50.959 38.391 1.00 49.16
    ATOM 1799 C GLU 391
     ATOM 1800 O GLU 391
                               68.463 52.055 38.956 1.00 58.82
     ATOM 1801 N CYA 392
                               67.802 50.782 37.224 1.00 49.75
                               67.255 51.908 36.475 1.00 45.56
    ATOM 1802 CA CYA 392
                                67.667 51.768 35.016 1.00 44.82
     ATOM 1803 CB CYA 392
50
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ATOM 1804 SG CYA 392
                              69.443 51.771 34.913 1.00 50.78
                                69.929 50.778 33.022 1.00 53.29
     ATOM 1805 AS CYA 392
                               65.771 52.200 36.601 1.00 44.35
     ATOM 1806 C CYA 392
    ATOM 1807 O CYA 392
                               64.988 51.324 36.962 1.00 44.10
     ATOM 1808 N PRO 393
                               65.378 53.469 36.365 1.00 45.52
     ATOM 1809 CD PRO 393
                              66.275 54.603 36.075 1.00 37.38
     ATOM 1810 CA PRO 393
                                63.982 53.916 36.444 1.00 45.41
    ATOM 1811 CB PRO 393
                               64.105 55.438 36.376 1.00 43.33
    ATOM 1812 CG PRO 393
                                65.329 55.644 35.542 1.00 39.89
    ATOM 1813 C PRO 393
                               63.108 53.376 35.318 1.00 44.89
10
                               63.556 53.239 34.175 1.00 45.60
     ATOM 1814 O PRO 393
    ATOM 1815 N THR 394
                               61.843 53.135 35.647 1.00 47.52
     ATOM 1816 CA THR 394
                                60.853 52.603 34.713 1.00 53.06
    ATOM 1817 CB THR 394
                                59.459 52.583 35.371 1.00 61.06
    ATOM 1818 OG1 THR 394
                                59.609 52.470 36.794 1.00 72.44
15
     ATOM 1819 CG2 THR 394
                                58.640 51.401 34.860 1.00 61.05
     ATOM 1820 C THR 394
                               60.767 53.373 33.392 1.00 49.98
                               60.507 52.786 32.339 1.00 51.06
     ATOM 1821 O THR 394
     ATOM 1822 N GLU 395
                               61.024 54.676 33.452 1.00 48.55
20
                                60.970 55.548 32.282 1.00 44.21
    ATOM 1823 CA GLU 395
                                61.258 56.987 32.697 1.00 41.66
    ATOM 1824 CB GLU 395
     ATOM 1825 C GLU 395
                               61.899 55.134 31.134 1.00 43.46
                               61.684 55.527 29.988 1.00 44.17
     ATOM 1826 O GLU 395
                               62.934 54.359 31.449 1.00 41.05
     ATOM 1827 N LEU 396
25
     ATOM 1828 CA LEU 396
                              63.898 53.899 30.448 1.00 39.55
    ATOM 1829 CB LEU 396
                               65.270 53.708 31.106 1.00 35.03
    ATOM 1830 CG LEU 396
                               66.296 54.834 30.945 1.00 40.06
                               65.638 56.200 31.055 1.00 39.06
     ATOM 1831 CD1 LEU 396
     ATOM 1832 CD2 LEU 396
                                67.398 54.669 31.978 1.00 32.78
                               63.468 52.602 29.757 1.00 38.50
30
    ATOM 1833 C LEU 396
    ATOM 1834 O LEU 396
                               64.106 52.150 28.804 1.00 34.72
                               62.364 52.028 30.225 1.00 38.76
    ATOM 1835 N PHE 397
    ATOM 1836 CA PHE 397
                               61.860 50.774 29.683 1.00 36.57
                               61.610 49.775 30.819 1.00 33.96
     ATOM 1837 CB PHE 397
    ATOM 1838 CG PHE 397
                                62.842 49.421 31.607 1.00 36.95
35
                                63.331 50.280 32.587 1.00 34.61
    ATOM 1839 CD1 PHE 397
                                63.523 48.234 31.362 1.00 37.14
    ATOM 1840 CD2 PHE 397
    ATOM 1841 CE1 PHE 397
                                64.481 49.964 33.310 1.00 31.57
     ATOM 1842 CE2 PHE 397
                                64.675 47.908 32.082 1.00 37.85
     ATOM 1843 CZ PHE 397
40
                               65.153 48.776 33.056 1.00 33.08
                               60.584 50.921 28.858 1.00 35.65
     ATOM 1844 C PHE 397
                               59.519 51.249 29.399 1.00 35.75
     ATOM 1845 O PHE 397
     ATOM 1846 N PRO 398
                               60.672 50.685 27.536 1.00 35.78
    ATOM 1847 CD PRO 398
                                61.891 50.367 26.767 1.00 32.81
     ATOM 1848 CA PRO 398
                                59.503 50.786 26.658 1.00 33.94
45
                                60.041 50.297 25.315 1.00 33.91
     ATOM 1849 CB PRO 398
     ATOM 1850 CG PRO 398
                                61.488 50.707 25.356 1.00 33.09
                               58.434 49.840 27.210 1.00 34.98
     ATOM 1851 C PRO 398
                               58.753 48.729 27.654 1.00 35.76
    ATOM 1852 O PRO 398
                               57.163 50.267 27.219 1.00 37.67
50
    ATOM 1853 N PRO 399
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56.661 51.578 26.776 1.00 38.02
     ATOM 1854 CD PRO 399
     ATOM 1855 CA PRO 399
                                56.070 49.433 27.733 1.00 36.86
                                54.803 50.183 27.291 1.00 34.14
     ATOM 1856 CB PRO 399
                                55.282 51.240 26.310 1.00 37.00
     ATOM 1857 CG PRO 399
                               56.085 47.970 27.273 1.00 37.06
     ATOM 1858 C PRO 399
 5
     ATOM 1859 O PRO 399
                               55.967 47.063 28.099 1.00 37.07
                               56.299 47.738 25.980 1.00 35.13
     ATOM 1860 N LEU 400
     ATOM 1861 CA LEU 400
                                56.327 46.374 25.445 1.00 35.86
     ATOM 1862 CB LEU 400
                                56.314 46.385 23.914 1.00 31.49
                                56.181 45.017 23.227 1.00 30.73
     ATOM 1863 CG LEU 400
10
                                54.901 44.330 23.674 1.00 21.35
     ATOM 1864 CD1 LEU 400
                                56.197 45.183 21.720 1.00 25.42
     ATOM 1865 CD2 LEU 400
     ATOM 1866 C LEU 400
                               57.542 45.597 25.958 1.00 36.51
                               57.458 44.392 26.219 1.00 37.47
     ATOM 1867 O LEU 400
                               58.671 46.290 26.095 1.00 32.26
15
     ATOM 1868 N PHE 401
     ATOM 1869 CA PHE 401
                                59.899 45.682 26.596 1.00 35.15
     ATOM 1870 CB PHE 401
                               61.014 46.739 26.648 1.00 35.99
                                62.346 46.213 27.117 1.00 39.41
     ATOM 1871 CG PHE 401
     ATOM 1872 CD1 PHE 401
                                62.845 45.003 26.639 1.00 35.94
20
     ATOM 1873 CD2 PHE 401
                                63.119 46.944 28.019 1.00 40.55
     ATOM 1874 CE1 PHE 401
                                64.088 44.531 27.055 1.00 30.16
                                64.367 46.478 28.439 1.00 35.53
     ATOM 1875 CE2 PHE 401
                               64.849 45.271 27.952 1.00 36.39
     ATOM 1876 CZ PHE 401
                               59.607 45.129 27.996 1.00 36.42
     ATOM 1877 C PHE 401
                               59.957 43.995 28.317 1.00 36.71
25
     ATOM 1878 O PHE 401
     ATOM 1879 N LEU 402
                               58.920 45.925 28.805 1.00 36.59
                              58.561 45.528 30.158 1.00 37.68
     ATOM 1880 CA LEU 402
     ATOM 1881 CB LEU 402
                                57.986 46.720 30.917 1.00 40.71
     ATOM 1882 CG LEU 402
                                58.963 47.751 31.463 1.00 43.13
                                58.180 48.926 32.031 1.00 39.88
     ATOM 1883 CD1 LEU 402
30
     ATOM 1884 CD2 LEU 402
                                59.847 47.103 32.527 1.00 38.39
     ATOM 1885 C LEU 402
                               57.521 44.420 30.164 1.00 38.02
     ATOM 1886 O LEU 402
                               57.582 43.507 30.984 1.00 37.39
     ATOM 1887 N GLU 403
                               56.558 44.522 29.251 1.00 39.74
                              55,469 43,559 29,166 1.00 42,79
35
     ATOM 1888 CA GLU 403
     ATOM 1889 CB GLU 403
                                54.445 44.022 28.129 1.00 46.21
     ATOM 1890 CG GLU 403
                                53.092 43.330 28.232 1.00 56.88
     ATOM 1891 CD GLU 403
                                52.090 43.833 27.202 1.00 65.21
     ATOM 1892 OE1 GLU 403
                                52.230 44.983 26.728 1.00 70.60
                                51.154 43.073 26.870 1.00 70.53
     ATOM 1893 OE2 GLU 403
40
                               55.890 42.121 28.886 1.00 40.14
     ATOM 1894 C GLU 403
                               55.368 41.200 29.506 1.00 40.57
     ATOM 1895 O GLU 403
     ATOM 1896 N VAL 404
                               56.835 41.932 27.966 1.00 39.43
     ATOM 1897 CA VAL 404
                               57.292 40.586 27.610 1.00 40.96
45
     ATOM 1898 CB VAL 404
                                57.851 40.516 26.159 1.00 35.50
     ATOM 1899 CG1 VAL 404
                                56.807 40.995 25.177 1.00 43.46
                                59.132 41.321 26.030 1.00 25.74
     ATOM 1900 CG2 VAL 404
     ATOM 1901 C VAL 404
                               58.317 39.946 28.536 1.00 41.94
     ATOM 1902 O VAL 404
                               58.468 38.722 28.533 1.00 43.82
                               59.026 40.759 29.310 1.00 39.84
     ATOM 1903 N PHE 405
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ATOM 1904 CA PHE 405
                                60.051 40.223 30.189 1.00 42.73
                                61.401 40.897 29.913 1.00 36.85
     ATOM 1905 CB PHE 405
                                61.963 40.596 28.551 1.00 33.23
     ATOM 1906 CG PHE 405
     ATOM 1907 CD1 PHE 405
                                 62.283 41.625 27.672 1.00 33.90
                                 62.157 39.281 28.138 1.00 31.62
     ATOM 1908 CD2 PHE 405
     ATOM 1909 CE1 PHE 405
                                62.786 41.351 26.399 1.00 39.16
                                62.657 38.997 26.872 1.00 33.33
     ATOM 1910 CE2 PHE 405
                                62,972 40,033 25,999 1.00 31.99
     ATOM 1911 CZ PHE 405
                               59.723 40.273 31.676 1.00 43.97
     ATOM 1912 C PHE 405
                               60.636 39.943 32.460 1.00 46.56
     ATOM 1913 O PHE 405
10
                               67.928 36.755 11.188 1.00 33.04
             1 O1 HOH 501
     ATOM
             2 O1 HOH 502
                               69.618 40.719 13.009 1.00 23.00
     ATOM
             3 O1 HOH 503
                               64.885 40.168 12.340 1.00 23.00
     ATOM
                               63.079 40.108 15.841 1.00 23.00
             4 O1 HOH 504
     ATOM
             5 O1 HOH 505
                               63.404 46.536 15.354 1.00 36.41
     ATOM
15
                               61.299 15.617 -0.595 1.00 23.00
             6 O1 HOH 506
     ATOM
                               67.359 15.375 0.551 1.00 23.00
             7 O1 HOH 507
     ATOM
                               67.230 12.002 -0.634 1.00 23.00
             8 O1 HOH 508
     ATOM
             9 O1 HOH 509
                               66.906 12.467 3.855 1.00 23.00
     ATOM
                               61.785 9.946 3.983 1.00 23.00
20
     ATOM
             10 O1 HOH 510
                               57.670 11.385 9.909 1.00 23.00
     ATOM
             11 O1 HOH 511
             12 O1 HOH 512
                                55.791 11.570 10.291 1.00 23.00
     ATOM
                                54.637 14.058 9.201 1.00 23.00
             13 O1 HOH 513
     ATOM
                                55.882 16.054 12.204 1.00 26.53
     ATOM
             14 O1 HOH 514
             15 O1 HOH 515
                                53.685 15.842 18.209 1.00 23.00
25
     ATOM
                               49.559 24.773 19.020 1.00 23.00
             16 O1 HOH 516
     ATOM
                                51.258 25.512 13.384 1.00 37.74
             17 O1 HOH 517
     ATOM
                                53.551 25.749 10.593 1.00 42.31
     ATOM
             18 O1 HOH 518
                                50.338 23.299 7.662 1.00 41.19
             19 O1 HOH 519
     ATOM
                                50.830 20.272 8.323 1.00 28.46
             20 O1 HOH 520
30
     ATOM
                                48.630 20.291 6.429 1.00 23.00
             21 O1 HOH 521
     ATOM
             22 O1 HOH 522
                                49.233 17.389 2.867 1.00 23.00
     ATOM
             23 O1 HOH 523
                                52.076 22.770 1.260 1.00 23.00
     ATOM
                                51.671 23.621 -1.020 1.00 23.00
             24 O1 HOH 524
     ATOM
             25 O1 HOH 525
                                58.294 31.509 2.147 1.00 31.83
35
     ATOM
                                57.497 36.071 2.268 1.00 23.00
     ATOM
             26 O1 HOH 526
                                65.373 36.025 6.809 1.00 23.00
             27 O1 HOH 527
     ATOM
                                67.871 36.399 6.419 1.00 66.52
             28 O1 HOH 528
     ATOM
                                67.189 33.811 9.409 1.00 23.00
             29 O1 HOH 529
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             37 O1 HOH 537
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     ATOM 2303 CH3 ACY 701
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     ATOM 2306 C3 IBR
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     ATOM 2307 C4 IBR
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     ATOM 2308 C5 IBR
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     ATOM 2309 C6 IBR
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     ATOM 2310 C7 IBR
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     ATOM 2311 C8 IBR
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                               67.383 42.244 24.921 1.00 26.78
     ATOM 2313 C10 IBR
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     ATOM 2315 C12 IBR
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     ATOM 2320 C17 IBR
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     ATOM 2321 C18 IBR
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     END
     END
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## APPENDIX 6

## TR\_T3.PDB

REMARK rTR\_t3 full length numbering

REMARK

5 REMARK Rfactor 0.221 Rfree 0.240

REMARK Resolution 5. 2.0 all reflections

REMARK conformation of MET 388 confirmed by SA omit map

**REMARK** 

REMARK Three cacodylate-modified cysteines (CYA)

10 REMARK Cya334, Cya380, Cya392

REMARK cacodylate modeled as single arsenic atom

REMARK

REMARK side chain of certain residues modeled as ALA due to poor density;

REMARK however, residue name reflects true residue for clarity

15 REMARK

REMARK clone obtained from Murray et. al.

REMARK deposited sequence confirmed,

REMARK differing from that reported by Thompson et. al.

REMARK in the following codons:

20 REMARK 281 Thr - Ala

REMARK 285 Lys - Glu

REMARK identical to that reported by Mitsuhashi et. al.

REMARK gb:RNTRAVI X07409

JRNL AUTH

M.B. MURRAY, N.D.ZILZ,

25 N.L.MCCREARY,M.J.MACDONALD

JRNL AUTH 2 H.C.TOWLE

JRNL TITL ISOLATION AND CHARACTERIZATION OF RAT CDNA CLONES FOR TWO

JRNL TITL 2 DISTINCT THYROID HORMONE RECPTORS

30 JRNL REF JBC

JRNL AUTH C.C.THOMPSON, C.WEINBERGER, R.LEBO, R.M.EVANS

JRNL TITL IDENTIFICATION OF A NOVEL THYROID HORMONE RECEPTOR EXPRESSED

V. 263 25 1988

JRNL TITL 2 IN THE MAMMALIAN CENTRAL NERVOUS SYSTEM

35 JRNL REF SCIENCE V. 237 1987

JRNL AUTH T.MITSUHASHI,G.TENNYSON,V.NIKODEM

JRNL TITL NUCLEOTIDE SEQUENCE OF NOVEL CDNAS GENERATED BY ALTERNATIVE

JRNL TITL 2 SPLICING OF A RAT THYROID HORMONE RECEPTOR

40 GENE TRANSCRIPT

JRNL REF NUC. ACIDS. RES. V. 16 12 1988 REMARK

ATOM 1 CB ARG 157 68.406 10.620 7.027 1.00 41.66

ATOM 2 CG ARG 157 69.926 10.540 6.997 1.00 44.48

45 ATOM 3 CD ARG 157 70.552 11.261 8.173 1.00 47.02

ATOM 4 NE ARG 157 70.112 10.680 9.435 1.00 49.73

ATOM 5 CZ ARG 157 70.917 10.392 10.450 1.00 51.21

ATOM 6 NH1 ARG 157 72.223 10.629 10.361 1.00 51.79

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    ATOM
             62 CD GLU 164
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            118 CG1 VAL 170
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                               56.692 28.234 9.182 1.00 18.34
                               57.375 27.102 9.946 1.00 17.05
     ATOM
            124 CB ALA 171
     ATOM 125 C ALA 171
                              57.733 29.151 8.533 1.00 17.84
                              58.084 30.200 9.091 1.00 18.67
20
     ATOM 126 O ALA 171
     ATOM
            127 N THR 172
                              58.231 28.756 7.367 1.00 17.81
     ATOM 128 CA THR 172
                               59.215 29.551 6.639 1.00 18.88
     ATOM 129 CB THR 172
                               59.726 28.794 5.380 1.00 20.47
     ATOM 130 OG1 THR 172
                                60.280 27.531 5.776 1.00 21.38
25
     ATOM 131 CG2 THR 172
                                60.806 29.599 4.648 1.00 20.22
                              58.655 30.932 6.251 1.00 19.42
     ATOM 132 C THR 172
     ATOM 133 O THR 172
                              59.320 31.957 6.435 1.00 17.98
     ATOM 134 N GLU 173
                               57.425 30.970 5.756 1.00 19.97
     ATOM 135 CA GLU 173
                               56.811 32.236 5.374 1.00 22.51
30
     ATOM 136 CB GLU 173
                               55.520 31.981 4.577 1.00 27.26
                               54.823 33.244 4.005 1.00 34.96
     ATOM 137 CG GLU 173
    ATOM 138 CD GLU 173
                               55.690 34.040 3.020 1.00 39.54
     ATOM 139 OE1 GLU 173
                                56.610 33.454 2.395 1.00 41.82
     ATOM 140 OE2 GLU 173
                                55,443 35.259 2.872 1.00 41.06
35
    ATOM 141 C GLU 173
                              56.538 33.099 6.622 1.00 21.60
     ATOM 142 O GLU 173
                               56.726 34.313 6.595 1.00 21.73
                              56.123 32.461 7.716 1.00 19.69
    ATOM 143 N ALA 174
    ATOM
           144 CA ALA 174
                               55.844 33.155 8.968 1.00 18.07
                               55.423 32.169 10.037 1.00 16.90
    ATOM 145 CB ALA 174
40
     ATOM 146 C ALA 174
                              57.101 33.883 9.400 1.00 17.65
                              57.052 35.031 9.829 1.00 19.80
     ATOM
            147 O ALA 174
    ATOM 148 N HIS 175
                              58.240 33.222 9.259 1.00 16.39
           149 CA HIS 175
                              59.498 33.831 9.629 1.00 16.41
    ATOM
    ATOM 150 CB HIS 175
                              60.574 32.758 9.804 1.00 12.71
    ATOM 151 CG HIS 175
                              61.938 33.318 10.043 1.00 11.09
45
    ATOM 152 CD2 HIS 175
                               62,373 34,252 10,920 1.00 8.26
    ATOM
           153 ND1 HIS 175
                               63.030 32.977 9.273 1.00 13.39
            154 CE1 HIS 175
                              64.076 33.683 9.658 1.00 13.77
    ATOM
            155 NE2 HIS 175
                               63.702 34.464 10.658 1.00 12.70
    ATOM
                             59.959 34.903 8.624 1.00 19.55
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    ATOM
           156 C HIS 175
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ATOM
            157 O HIS 175
                              60.293 36.027 9.016 1.00 18.38
                               59.987 34.555 7.339 1.00 20.77
            158 N ARG 176
     ATOM
                                60.424 35.494 6.307 1.00 21.30
     ATOM
            159 CA ARG 176
                               60.315 34.876 4.917 1.00 24.87
     ATOM
            160 CB ARG 176
                                61.361 33.827 4.609 1.00 30.22
     ATOM
            161 CG ARG 176
            162 CD ARG 176
                                61.429 33.603 3.116 1.00 36.29
     ATOM
     ATOM
            163 NE ARG 176
                                62.256 32.457 2.758 1.00 44.72
            164 CZ ARG 176
                               62.031 31.680 1.700 1.00 49.80
     ATOM
     ATOM
            165 NHI ARG 176
                                61.000 31.935 0.894 1.00 50.83
                                62.812 30.627 1.466 1.00 50.14
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     ATOM
            166 NH2 ARG 176
                               59.658 36.807 6.337 1.00 20.67
     ATOM
            167 C ARG 176
                               60.256 37.877 6.238 1.00 20.53
     ATOM
            168 O ARG 176
            169 N SER 177
                              58.344 36.730 6.508 1.00 20.67
     ATOM
     ATOM
            170 CA SER 177
                               57.526 37.934 6.551 1.00 21.86
            171 CB SER 177
                               56.061 37.588 6.298 1.00 19.59
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     ATOM
            172 OG SER 177
                               55.541 36.774 7.329 1.00 21.85
     ATOM
            173 C SER 177
                              57.659 38.733 7.857 1.00 23.27
     ATOM
     ATOM
            174 O SER 177
                              57.073 39.807 7.989 1.00 24.40
            175 N THR 178
                               58.383 38.202 8.837 1.00 22.16
     ATOM
                               58.542 38.913 10.095 1.00 20.62
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     ATOM
            176 CA THR 178
                               57.853 38.162 11.265 1.00 19.93
     ATOM
            177 CB THR 178
            178 OG1 THR 178
                                58.386 36.838 11.381 1.00 18.72
     ATOM
                                56,359 38.057 11.033 1.00 16.95
            179 CG2 THR 178
     ATOM
                               60.015 39.137 10.394 1.00 21.57
     ATOM
            180 C THR 178
25
     ATOM
            181 O THR 178
                               60.368 39.649 11.449 1.00 23.91
                               60.870 38.769 9.445 1.00 22.22
     ATOM
            182 N ASN 179
                               62.316 38.912 9.585 1.00 24.22
     ATOM
            183 CA ASN 179
                               63.013 37.690 8.970 1.00 22.49
     ATOM
            184 CB ASN 179
            185 CG ASN 179
                               64.480 37.596 9.344 1.00 23.53
     ATOM
            186 OD1 ASN 179
                                64.866 37.912 10.464 1.00 22.32
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     ATOM
            187 ND2 ASN 179
                                65.296 37.100 8.425 1.00 23.84
     ATOM
                               62.744 40.210 8.881 1.00 26.52
     ATOM
            188 C ASN 179
            189 O ASN 179
                               62.923 40.253 7.657 1.00 26.65
     ATOM
                               62.898 41.267 9.671 1.00 27.47
            190 N ALA 180
     ATOM
                              63.255 42.582 9.166 1.00 30.30
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     ATOM
            191 CA ALA 180
                               63.552 43.508 10.321 1.00 27.21
     ATOM
            192 CB ALA 180
                               64.404 42.593 8.166 1.00 33.14
     ATOM
            193 C ALA 180
     ATOM
            194 O ALA 180
                               65.440 41.972 8.397 1.00 33.71
                               64.209 43.295 7.049 0.50 35.09
            195 N GLN 181
                                                             ALTA
     ATOM
40
     ATOM
            196 CA GLN 181
                               65.212 43.423 5.980 0.50 37.44
                                                              ALTA
                               66.544 43.974 6.511 0.50 38.60
     ATOM
            197 CB GLN 181
                                                              ALTA
                               66.728 45.462 6.299 0.50 40.53
                                                              ALTA
            198 CG GLN 181
     ATOM
            199 CD GLN 181
     ATOM
                               65.805 46.291 7.162 0.50 42.72
                                                              ALTA
     ATOM
            200 OE1 GLN 181
                                64.639 46.512 6.828 0.50 42.05
                                                              ALTA
            201 NE2 GLN 181
                                66,324 46,756 8,284 0,50 44,59
                                                              ALTA
45
     ATOM
                               65.481 42.180 5.138 0.50 38.43
            202 C GLN 181
                                                             ALTA
     ATOM
     ATOM
            203 O GLN 181
                               66.175 42.262 4.118 0.50 38.92
                                                             ALTA
            204 N GLY 182
                               64.958 41.034 5.562 1.00 38.74
     ATOM
                               65.166 39.808 4.805 1.00 40.07
            205 CA GLY 182
     ATOM
                               66.634 39.554 4.486 1.00 42.06
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     ATOM
            206 C GLY 182
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ATOM
            207 O GLY 182
                             67.504 39.684 5.346 1.00 43.28
            208 N SER 183
                             66.926 39.272 3.224 1.00 43.72
    ATOM
                             68.299 39.001 2.812 1.00 45.88
            209 CA SER 183
    ATOM
                              68.304 38.069 1.593 1.00 47.26
    ATOM
            210 CB SER 183
                            67.519 38.605 0.531 1.00 47.23
5
    ATOM
            211 OG SER 183
    ATOM 212 C SER 183
                             69.095 40.268 2.497 1.00 46.24
                             70.290 40.194 2.185 1.00 48.13
    ATOM 213 O SER 183
                             68.445 41.426 2.579 1.00 45.79
    ATOM 214 N HIS 184
    ATOM 215 CA HIS 184
                            69.111 42.690 2.276 1.00 45.00
    ATOM 216 CB HIS 184
                              68.127 43.636 1.594 1.00 43.54
10
                             69.732 43.351 3.516 1.00 44.67
    ATOM 217 C HIS 184
    ATOM 218 O HIS 184
                             70.316 44.440 3.428 1.00 45.02
    ATOM 219 N TRP 185
                             69.659 42.663 4.653 1.00 43.24
                             70.190 43.172 5.919 1.00 40.98
    ATOM 220 CA TRP 185
                              70.078 42.106 7.020 1.00 37.96
    ATOM 221 CB TRP 185
15
    ATOM 222 CG TRP 185
                              70.889 40.874 6.775 1.00 34.14
    ATOM 223 CD2 TRP 185
                               72.197 40.593 7.291 1.00 33.38
                               72.572 39.321 6.807 1.00 31.68
    ATOM 224 CE2 TRP 185
            225 CE3 TRP 185
                               73.092 41.296 8.107 1.00 31.65
    ATOM
    ATOM 226 CD1 TRP 185
                               70.530 39.790 6.028 1.00 34.27
20
            227 NE1 TRP 185
                               71.536 38.852 6.043 1.00 33.51
    ATOM
            228 CZ2 TRP 185
                               73.795 38.733 7.121 1.00 31.67
    ATOM
                               74.308 40.713 8.419 1.00 31.29
    ATOM 229 CZ3 TRP 185
                               74.651 39.444 7.923 1.00 31.06
    ATOM 230 CH2 TRP 185
    ATOM
            231 C TRP 185
                             71.618 43.720 5.856 1.00 41.52
25
                              71.893 44.817 6.335 1.00 40.52
    ATOM 232 O TRP 185
                              72.520 42.976 5.234 1.00 42.94
    ATOM 233 N LYS 186
                              73.896 43.417 5.143 1.00 45.25
    ATOM
            234 CA LYS 186
            235 CB LYS 186
                              74.764 42.328 4.508 1.00 45.96
    ATOM
                              76.255 42.600 4.590 1.00 48.07
            236 CG LYS 186
30
    ATOM
            237 CD LYS 186
                              77.053 41.307 4.504 1.00 51.20
    ATOM
                              78.554 41.574 4.457 1.00 52.69
            238 CE LYS 186
    ATOM
            239 NZ LYS 186
                              78.975 42.277 3.201 1.00 55.56
    ATOM
                              74.025 44.730 4.377 1.00 47.38
            240 C LYS 186
    ATOM
            241 O LYS 186
                              74.914 45.535 4.663 1.00 47.65
    ATOM
35
            242 N GLN 187
                              73.134 44.959 3.418 0.50 48.02
                                                            ALTA
    ATOM
            243 CA GLN 187
                              73.193 46.183 2.623 0.50 48.69
                                                            ALTA
    ATOM
                               72.547 45.973 1.246 0.50 48.66
    ATOM 244 CB GLN 187
                                                            ALTA
                               73.104 44.771 0.453 0.50 49.05
                                                            ALTA
    ATOM 245 CG GLN 187
                               74.624 44.766 0.339 0.50 49.17
                                                            ALTA
40
    ATOM 246 CD GLN 187
                               75.225 45.691 -0.209 0.50 49.71
    ATOM 247 OE1 GLN 187
                                                             ALTA
            248 NE2 GLN 187
                               75.250 43.710 0.847 0.50 48.57
                                                             ALTA
    ATOM
                              72.551 47.373 3.343 0.50 49.06
                                                            ALTA
            249 C GLN 187
    ATOM
    ATOM
            250 O GLN 187
                              73.094 48.475 3.329 0.50 49.53
                                                            ALTA
            251 N ARG 188
                              71.405 47.152 3.980 1.00 49.18
45
    ATOM
                               70.723 48.221 4.695 1.00 49.90
            252 CA ARG 188
    ATOM
    ATOM
            253 CB ARG 188
                               69.209 47.988 4.653 1.00 53.68
            254 CG ARG 188
                               68.617 47.798 3.251 1.00 57.22
    ATOM
                               67.099 47.962 3.302 1.00 60.67
           255 CD ARG 188
    ATOM
                               66.430 47.441 2.110 1.00 64.43
    ATOM 256 NE ARG 188
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65.931 46.208 2.009 1.00 66.13
            257 CZ ARG 188
    ATOM
                                66.027 45.362 3.031 1.00 66.69
            258 NH1 ARG 188
    ATOM
                                65.318 45.823 0.893 1.00 66.10
           259 NH2 ARG 188
    ATOM
                              71.150 48.510 6.133 1.00 48.42
           260 C ARG 188
    ATOM
                               70.544 49.368 6.784 1.00 48.86
    ATOM
            261 O ARG 188
                               72.153 47.804 6.647 1.00 46.00
    ATOM
           262 N ARG 189
                               72.581 48.030 8.028 1.00 44.24
           263 CA ARG 189
    ATOM
                               73.039 46.726 8.690 1.00 43.40
           264 CB ARG 189
    ATOM
                               74.367 46.204 8.203 1.00 43.05
           265 CG ARG 189
    ATOM
                               74.808 45.021 9.019 1.00 43.62
    ATOM 266 CD ARG 189
10
                               76.185 44.660 8.717 1.00 45.95
    ATOM 267 NE ARG 189
                               76.981 43.976 9.536 1.00 48.56
    ATOM 268 CZ ARG 189
    ATOM 269 NH1 ARG 189
                                76.548 43.560 10.724 1.00 46.34
                                78.233 43.735 9.174 1.00 50.12
           270 NH2 ARG 189
    ATOM
                              73.642 49.116 8.238 1.00 43.20
    ATOM 271 C ARG 189
15
                               74.629 49.210 7.500 1.00 43.07
           272 O ARG 189
    ATOM
                              73.427 49.925 9.268 1.00 41.56
    ATOM
           273 N LYS 190
                               74.335 51.003 9.628 1.00 39.96
    ATOM 274 CA LYS 190
    ATOM 275 CB LYS 190
                               73.563 52.323 9.757 1.00 38.85
                              74.983 50.631 10.956 1.00 38.91
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    ATOM
           276 C LYS 190
           277 O LYS 190
                              74.345 50.015 11.806 1.00 38.17
    ATOM
    ATOM 278 N PHE 191
                              76.261 50.959 11.104 1.00 38.49
                               76.998 50.673 12.326 1.00 38.42
           279 CA PHE 191
    ATOM
                               78.500 50.762 12.073 1.00 38.37
    ATOM 280 CB PHE 191
25
           281 CG PHE 191
                               79.056 49.608 11.308 1.00 39.05
    ATOM
                               78.712 49.408 9.976 1.00 40.02
           282 CD1 PHE 191
    ATOM
                               79.942 48.727 11.917 1.00 39.19
    ATOM 283 CD2 PHE 191
                               79.245 48.344 9.256 1.00 40.57
    ATOM 284 CE1 PHE 191
    ATOM 285 CE2 PHE 191
                               80.482 47.661 11.213 1.00 40.32
                               80.133 47.466 9.875 1.00 41.84
    ATOM 286 CZ PHE 191
30
                              76.650 51.673 13.416 1.00 37.96
    ATOM 287 C PHE 191
                              76.568 52.872 13.151 1.00 38.95
    ATOM 288 O PHE 191
                              76.433 51.184 14.634 1.00 37.05
    ATOM 289 N LEU 192
                               76.138 52.063 15.759 1.00 35.99
    ATOM 290 CA LEU 192
                               75.833 51.247 17.014 1.00 33.04
    ATOM 291 CB LEU 192
35
    ATOM 292 CG LEU 192
                               75.503 52.074 18.260 1.00 31.38
    ATOM 293 CD1 LEU 192
                                74.116 52.651 18.102 1.00 29.02
                                75.592 51.229 19.536 1.00 30.32
    ATOM 294 CD2 LEU 192
                              77.436 52.831 15.976 1.00 36.99
    ATOM 295 C LEU 192
                              78.500 52.218 16.112 1.00 37.66
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     ATOM 296 O LEU 192
                              77.377 54.177 15.988 1.00 38.15
     ATOM 297 N PRO 193
                               76.156 54.996 15.902 1.00 37.90
     ATOM 298 CD PRO 193
                               78.561 55.025 16.187 1.00 38.68
           299 CA PRO 193
     ATOM
                               77.950 56.365 16.568 1.00 37.20
     ATOM
            300 CB PRO 193
                               76.711 56.397 15.758 1.00 37.08
            301 CG PRO 193
45
     ATOM
                              79.475 54.503 17.294 1.00 41.12
            302 C PRO 193
     ATOM
            303 O PRO 193
                              79.005 54.129 18.367 1.00 42.26
     ATOM
            304 N ASP 194
                              80.782 54.509 17.052 1.00 43.62
     ATOM
                              81.731 54.012 18.050 1.00 46.71
            305 CA ASP 194
     ATOM
                               83.131 53.938 17.470 1.00 49.32
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     ATOM
            306 CB ASP 194
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83.237 52.904 16.397 1.00 52.34
            307 CG ASP 194
    ATOM
                                83.539 51.726 16.719 1.00 53.18
            308 OD1 ASP 194
    ATOM
                                82.981 53.268 15.227 1.00 55.10
            309 OD2 ASP 194
    ATOM
                              81.769 54.743 19.386 1.00 47.12
            310 C ASP 194
    ATOM
                              82.158 54.163 20.403 1.00 48.16
    ATOM
            311 O ASP 194
            312 N ASP 195
                              81.389 56.015 19.386 1.00 47.54
    ATOM
                               81.382 56.791 20.620 1.00 48.68
            313 CA ASP 195
    ATOM
                               81.180 58.285 20.322 1.00 50.76
    ATOM
            314 CB ASP 195
                               79.871 58.572 19.602 1.00 54.24
            315 CG ASP 195
    ATOM
                                78.929 59.082 20.253 1.00 56.17
            316 OD1 ASP 195
    ATOM
10
                                79.786 58.292 18.385 1.00 56.08
    ATOM
            317 OD2 ASP 195
                              80.304 56.274 21.580 1.00 47.63
    ATOM 318 C ASP 195
            319 O ASP 195
                              80.294 56.621 22.772 1.00 49.07
    ATOM
                              79,400 55,444 21,065 1,00 44,87
            320 N ILE 196
    ATOM
                               78.330 54.890 21.888 1.00 42.53
            321 CA ILE 196
    ATOM
15
                               76.983 54.813 21.121 1.00 42.19
            322 CB ILE 196
     ATOM
                               75.870 54.357 22.060 1.00 40.29
     ATOM 323 CG2 ILE 196
                               76.635 56.191 20.535 1.00 41.32
     ATOM 324 CG1 ILE 196
     ATOM 325 CD1 ILE 196
                               75.344 56.219 19.732 1.00 41.32
                              78.725 53.509 22.391 1.00 40.89
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     ATOM
            326 C ILE 196
                              79.358 52.722 21.679 1.00 40.08
     ATOM
            327 O ILE 196
            328 N GLY 197
                               78,384 53.240 23.642 1.00 40.16
     ATOM
                                78.705 51.957 24.228 1.00 40.21
            329 CA GLY 197
     ATOM
                               80.066 51.907 24.879 1.00 40.18
     ATOM
            330 C GLY 197
            331 O GLY 197
                               80.512 50.839 25.267 1.00 40.55
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     ATOM
                               80.718 53.057 25.029 1.00 41.25
            332 N GLN 198
     ATOM
                                82.038 53.111 25.664 1.00 40.94
            333 CA GLN 198
     ATOM
            334 CB GLN 198
                                83.041 53.823 24.738 1.00 39.51
     ATOM
            335 C GLN 198
                               81.995 53.796 27.046 1.00 40.93
     ATOM
                               83.036 54.197 27.571 1.00 41.83
            336 O GLN 198
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            337 N SER 199
                               80.806 53.859 27.654 1.00 39.68
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                               80.615 54.510 28.961 1.00 37.74
            338 CA SER 199
     ATOM
                               79.995 55.905 28.768 1.00 38.50
            339 CB SER 199
     ATOM
                               80.687 56.672 27.792 1.00 40.71
            340 OG SER 199
     ATOM
                               79.743 53.726 29.958 1.00 36.31
            341 C SER 199
35
     ATOM
                               78.719 54.228 30.436 1.00 35.69
            342 O SER 199
     ATOM
                               80.123 52.484 30.280 1.00 35.05
            343 N PRO 200
     ATOM
                                81.246 51.684 29.760 1.00 33.97
            344 CD PRO 200
     ATOM
                                79.313 51.715 31.228 1.00 35.89
            345 CA PRO 200
     ATOM
                                79.872 50.304 31.075 1.00 33.94
            346 CB PRO 200
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     ATOM
                                81.297 50.532 30.708 1.00 33.31
            347 CG PRO 200
     ATOM
                               79.477 52.241 32.656 1.00 37.75
            348 C PRO 200
     ATOM
                               80.484 51.959 33.299 1.00 38.78
            349 O PRO 200
     ATOM
                              78.493 52.988 33.158 1.00 39.61
     ATOM
            350 N ILE 201
                               78.590 53.551 34.511 1.00 40.56
            351 CA ILE 201
45
     ATOM
                               78.715 55.093 34.484 1.00 40.20
     ATOM 352 CB ILE 201
            353 CG2 ILE 201
                               80.125 55.501 34.082 1.00 41.06
     ATOM
                               77.690 55.694 33.532 1.00 40.98
            354 CG1 ILE 201
     ATOM
                               77.969 57.147 33.205 1.00 44.31
             355 CD1 ILE 201
     ATOM
                              77.535 53.160 35.546 1.00 41.40
            356 C ILE 201
     ATOM
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ATOM
            357 O ILE 201
                              77.768 53.313 36.751 1.00 42.09
                               76.365 52.701 35.104 1.00 41.42
     ATOM
            358 N VAL 202
                               75.325 52.293 36.053 1.00 40.70
    ATOM
            359 CA VAL 202
                               73.913 52.292 35.422 1.00 38.44
    ATOM
            360 CB VAL 202
                                72.881 51.826 36.435 1.00 35.91
    ATOM
            361 CG1 VAL 202
            362 CG2 VAL 202
                                73.560 53.692 34.934 1.00 36.42
    ATOM
            363 C VAL 202
                               75.687 50.917 36.622 1.00 41.64
    ATOM
            364 O VAL 202
                               76.094 50.008 35.894 1.00 42.05
    ATOM
    ATOM
            365 N SER 203
                              75.596 50.800 37.938 1.00 43.06
            366 CA SER 203
                               75.947 49.576 38.639 1.00 44.57
    ATOM
10
                               75.916 49.842 40.154 1.00 46.82
            367 CB SER 203
     ATOM
            368 OG SER 203
                               76.457 48.772 40.916 1.00 50.18
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            369 C SER 203
                              75.052 48.388 38.294 1.00 44.08
     ATOM
                              73.849 48.534 38.093 1.00 44.28
            370 O SER 203
    ATOM
    ATOM
            371 N MET 204
                               75.656 47.210 38.231 1.00 43.11
15
            372 CA MET 204
                               74.930 45.980 37.963 1.00 43.12
     ATOM
            373 CB MET 204
                               75.048 45.557 36.494 1.00 41.07
     ATOM
                                74.126 46.320 35.554 1.00 36.96
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            374 CG MET 204
            375 SD MET 204
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            376 CE MET 204
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            391 OD2 ASP 206
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            400 CB ASP 208
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     ATOM
            403 OD2 ASP 208
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    ATOM 413 CB VAL 210
            414 CG1 VAL 210
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            421 CG ASP 211
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     ATOM 423 OD2 ASP 211
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     ATOM 425 O ASP 211
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            427 CA LEU 212
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            428 CB LEU 212
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     ATOM 429 CG LEU 212
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            430 CD1 LEU 212
     ATOM
     ATOM 431 CD2 LEU 212
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            432 C LEU 212
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                               73.370 55.589 27.407 1.00 32.21
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            437 CG GLU 213
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            438 CD GLU 213
                                75.316 58.101 23.545 1.00 44.21
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            439 OE1 GLU 213
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                               72.966 54.801 25.111 1.00 31.91
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                               72.064 54.775 24.273 1.00 31.31
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            443 N ALA 214
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                                73.769 52.585 24.482 1.00 30.43
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            444 CA ALA 214
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            445 CB ALA 214
            446 C ALA 214
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            447 O ALA 214
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                               70.882 51.116 26.492 1.00 29.05
            449 CA PHE 215
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                               70.732 51.240 28.005 1.00 25.98
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            450 CB PHE 215
            451 CG PHE 215
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                                69.330 49.344 28.854 1.00 26.16
            452 CD1 PHE 215
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                                68.349 51.519 28.737 1.00 25.04
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            453 CD2 PHE 215
                                68.144 48.831 29.370 1.00 25.73
            454 CE1 PHE 215
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                                67.160 51.018 29.252 1.00 25.84
            455 CE2 PHE 215
     ATOM
                               67.058 49.669 29.570 1.00 25.25
            456 CZ PHE 215
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            458 O PHE 215
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                               69.714 53.108 25.776 1.00 31.41
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                               68.667 53.887 25.136 1.00 31.23
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                               68.976 55.375 25.256 1.00 32.50
            461 CB SER 216
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    ATOM
            462 OG SER 216
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            463 C SER 216
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            464 O SER 216
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            467 CB GLU 217
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            468 CG GLU 217
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            469 CD GLU 217
            470 OE1 GLU 217
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            471 OE2 GLU 217
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            472 C GLU 217
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            473 O GLU 217
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            476 CB PHE 218
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            477 CG PHE 218
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            478 CD1 PHE 218
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            479 CD2 PHE 218
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            480 CE1 PHE 218
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            481 CE2 PHE 218
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            482 CZ PHE 218
                               73.804 48.236 21.772 1.00 24.45
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                               66.658 48.985 21.409 1.00 27.98
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            485 N THR 219
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                                65.379 50.304 25.195 1.00 27.35
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            488 OG1 THR 219
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            489 CG2 THR 219
            490 C THR 219
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            491 O THR 219
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            494 CB LYS 220
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            496 O LYS 220
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            498 CA ILE 221
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            499 CB ILE 221
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            500 CG2 ILE 221
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            501 CG1 ILE 221
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            503 C ILE 221
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                               63.279 46.934 20.665 1.00 27.22
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            506 CA ILE 222
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            508 CG2 ILE 222
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            509 CG1 ILE 222
                                63.949 45.065 22.230 1.00 24.15
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                                64.727 44.610 23.458 1.00 21.43
            510 CD1 ILE 222
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                              61.797 46.614 20.519 1.00 28.33
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            511 C ILE 222
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                               61.445 45.459 20.260 1.00 29.81
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                                59.494 47.366 20.505 1.00 26.83
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            516 OG1 THR 223
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            518 C THR 223
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            522 CA PRO 224
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            523 CB PRO 224
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            524 CG PRO 224
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            526 O PRO 224
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            529 CB ALA 225
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            531 O ALA 225
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             535 CG2 ILE 226
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                                60.361 42.915 22.123 1.00 17.07
            536 CG1 ILE 226
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                                60.175 43.775 23.351 1.00 14.65
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            538 C ILE 226
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            539 O ILE 226
            540 N THR 227
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                                56.278 42.782 17.881 1.00 21.19
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            543 OG1 THR 227
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            544 CG2 THR 227
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            545 C THR 227
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            547 N ARG 228
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            550 CG ARG 228
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            551 CD ARG 228
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            552 NE ARG 228
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                                62.209 42.413 13.468 1.00 28.20
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            553 CZ ARG 228
             554 NH1 ARG 228
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            556 C ARG 228
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           561 CG1 VAL 229
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           562 CG2 VAL 229
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                               53.896 39.327 18.897 1.00 18.60
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     ATOM 568 CG1 VAL 230
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     ATOM 569 CG2 VAL 230
                                54.445 39.629 20.299 1.00 17.82
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                              53.115 36.863 16.828 1.00 18.46
     ATOM 571 O VAL 230
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                               52.704 40.953 14.586 1.00 24.23
     ATOM 576 OD1 ASP 231
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     ATOM 577 OD2 ASP 231
     ATOM 578 C ASP 231
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     ATOM 583 CG PHE 232
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     ATOM 584 CD1 PHE 232
     ATOM 585 CD2 PHE 232
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     ATOM 587 CE2 PHE 232
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     ATOM 589 C PHE 232
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     ATOM 599 CG LYS 234
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     ATOM 601 CE LYS 234
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     ATOM 604 O LYS 234
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     ATOM
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     ATOM 606 CA LYS 235
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607 CB LYS 235
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                               52.051 35.269 10.644 1.00 26.92
            608 CG LYS 235
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     ATOM 609 CD LYS 235
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            611 NZ LYS 235
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                              51.540 31.588 11.722 1.00 27.93
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    ATOM 613 O LYS 235
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    ATOM 616 CB LEU 236
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    ATOM 617 CG LEU 236
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    ATOM 619 CD2 LEU 236
    ATOM 620 C LEU 236
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    ATOM 621 O LEU 236
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    ATOM 622 N PRO 237
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    ATOM 624 CA PRO 237
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     ATOM 625 CB PRO 237
    ATOM 626 CG PRO 237
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    ATOM 627 C PRO 237
                              48.582 26.720 14.447 1.00 37.82
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                              47.629 27.102 15.125 1.00 37.08
                               49.495 25.893 14.935 1.00 40.42
    ATOM 629 N MET 238
    ATOM 630 CA MET 238
                               49.366 25.350 16.285 1.00 43.00
                               50.453 24.298 16.549 1.00 45.20
    ATOM 631 CB MET 238
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    ATOM 632 CG MET 238
                               50.043 22.837 16.296 1.00 47.16
                               50.598 22.117 14.725 1.00 52.25
    ATOM 633 SD MET 238
    ATOM 634 CE MET 238
                               52.305 21.809 15.033 1.00 47.29
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                              49.389 26.389 17.414 1.00 43.25
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    ATOM 639 CB PHE 239
                               51.031 29.615 17.765 1.00 32.40
    ATOM 640 CG PHE 239
                               51.293 30.673 18.795 1.00 27.12
    ATOM 641 CD1 PHE 239
                               52.099 30.398 19.893 1.00 24.57
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                               50.705 31.933 18.686 1.00 24.70
    ATOM 642 CD2 PHE 239
    ATOM 643 CE1 PHE 239
                               52.319 31.356 20.876 1.00 25.09
                               50.915 32.901 19.659 1.00 25.90
    ATOM 644 CE2 PHE 239
    ATOM 645 CZ PHE 239
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    ATOM 649 CA SER 240
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    ATOM 650 CB SER 240
                               46.534 31.706 16.094 1.00 38.34
    ATOM 651 C SER 240
                              45.627 30.304 17.981 1.00 37.30
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    ATOM 652 O SER 240
                              44.680 30.941 18.433 1.00 36.95
                              45.639 28.974 17.917 1.00 37.73
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    ATOM 654 CA GLU 241
                               44.531 28.155 18.418 1.00 38.44
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            656 CG GLU 241
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            659 OE2 GLU 241
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                               43.561 27.868 20.598 1.00 36.01
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                               45.959 28.296 21.920 1.00 31.31
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                              45.223 29.390 22.676 1.00 30.10
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                               44.783 27.843 24.674 1.00 28.53
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                               44.183 30.200 24.640 1.00 31.01
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    ATOM 673 CB PRO 243
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                               44.640 28.300 26.093 1.00 29.25
    ATOM
           674 CG PRO 243
                              45.195 31.356 24.774 1.00 31.71
    ATOM 675 C PRO 243
            676 O PRO 243
                              46.412 31.128 24.840 1.00 30.69
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     ATOM
                              44.694 32.585 24.804 1.00 32.36
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            678 CA CYS 244
                               45.539 33.763 24.920 1.00 33.57
    ATOM 679 CB CYS 244
                               44.675 35.028 25.050 1.00 37.62
                               45.262 36.418 24.022 1.00 51.95
    ATOM 680 SG CYS 244
                              46.536 33.660 26.081 1.00 31.12
    ATOM 681 C CYS 244
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                              47.677 34.087 25.942 1.00 30.37
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            683 N GLU 245
                               46.124 33.045 27.194 1.00 30.00
    ATOM
                               46.993 32.877 28.366 1.00 29.62
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    ATOM 685 CB GLU 245
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    ATOM 686 CG GLU 245
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                                43.882 32.940 29.860 1.00 37.87
    ATOM 687 CD GLU 245
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    ATOM 688 OE1 GLU 245
    ATOM 689 OE2 GLU 245
                                43.639 32.813 28.634 1.00 39.63
                               48.239 32.077 28.030 1.00 28.34
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                               49.322 32.343 28.557 1.00 27.88
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            692 N ASP 246
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                               49.182 30.212 26.798 1.00 25.23
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    ATOM
            694 CB ASP 246
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            695 CG ASP 246
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            696 OD1 ASP 246
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            697 OD2 ASP 246
                                47.712 26.824 26.696 1.00 31.38
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                              50.065 30.983 25.826 1.00 23.57
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            698 C ASP 246
            699 O ASP 246
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                               49.431 31.630 24.852 1.00 23.23
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    ATOM
            701 CA GLN 247
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            702 CB GLN 247
                                49.159 33.178 22.991 1.00 22.06
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                                48.329 32.307 22.066 1.00 22.74
            703 CG GLN 247
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                                47.435 33.141 21.169 1.00 24.91
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            704 CD GLN 247
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            705 OE1 GLN 247
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            706 NE2 GLN 247
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             711 CB ILE 248
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            713 CG1 ILE 248
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             714 CD1 ILE 248
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                                48.413 37.323 27.341 1.00 23.84
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             721 CG1 ILE 249
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             722 CD1 ILE 249
                                51.252 30.911 31.175 1.00 25.03
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     ATOM
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                              54.481 32.148 27.470 1.00 22.24
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            724 O ILE 249
                               55.677 32.321 27.733 1.00 22.90
             725 N LEU 250
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     ATOM
            730 CD2 LEU 250
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            752 C GLY 253
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                               60.397 32.429 26.292 1.00 23.10
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            753 O GLY 253
                               61.568 32.165 26.585 1.00 25.12
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            758 C CYS 254
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                               60.404 38.957 22.735 1.00 22.22
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            765 O CYS 255
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            769 CG MET 256
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            773 O MET 256
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            777 CG GLU 257
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            788 CD1 ILE 258
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            794 CG MET 259
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     ATOM
             806 CA LEU 261
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            812 O LEU 261
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                               72.837 38.063 14.475 1.00 19.40
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            829 N ALA 264
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            835 CA VAL 265
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            838 CG2 VAL 265
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            839 C VAL 265
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            849 NH2 ARG 266
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            851 O ARG 266
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            863 O TYR 267
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    ATOM 875 CB PRO 269
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    ATOM 876 CG PRO 269
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                              83.656 38.613 10.019 1.00 40.96
            878 O PRO 269
                              84.586 38.929 10.760 1.00 42.23
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    ATOM 879 N ALA 270
                               83.418 39.209 8.854 1.00 41.92
    ATOM 880 CA ALA 270
                               84.277 40.272 8.342 1.00 42.08
                               83.709 40.838 7.029 1.00 42.64
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    ATOM 881 CB ALA 270
    ATOM 882 C ALA 270
                              84.495 41.394 9.355 1.00 41.70
                               85.632 41.709 9.684 1.00 42.25
    ATOM 883 O ALA 270
                              83.408 41.970 9.865 1.00 41.87
    ATOM 884 N SER 271
    ATOM 885 CA SER 271
                               83.495 43.073 10.830 1.00 40.75
                               82.454 44.143 10.500 1.00 40.60
    ATOM 886 CB SER 271
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    ATOM 887 OG SER 271
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                              83,484 43,487 13.194 1.00 38.77
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            889 O SER 271
            890 N ASP 272
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    ATOM 891 CA ASP 272
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    ATOM 893 CG ASP 272
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    ATOM 894 OD1 ASP 272
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                              81.744 41.634 14.536 1.00 36.92
    ATOM
            896 C ASP 272
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    ATOM
            897 O ASP 272
                              81.907 42.156 15.648 1.00 37.56
    ATOM 898 N THR 273
                              80.603 41.723 13.865 1.00 33.65
            899 CA THR 273
                               79.469 42.443 14.425 1.00 31.57
    ATOM
            900 CB THR 273
                               79.246 43.790 13.695 1.00 31.69
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            901 OG1 THR 273
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            902 CG2 THR 273
                                80.426 44.730 13.922 1.00 31.53
    ATOM
            903 C THR 273
                              78.184 41.631 14.310 1.00 30.15
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    ATOM
            904 O THR 273
                              78.104 40.697 13.504 1.00 30.10
                              77.213 41.942 15.164 1.00 27.09
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                              75.907 41.303 15.103 1.00 25.94
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    ATOM
            906 CA LEU 274
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            908 CG LEU 274
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                                75.436 39.631 18.602 1.00 21.14
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            910 CD2 LEU 274
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    ATOM
            911 C LEU 274
            912 O LEU 274
                               75.339 43.557 14.568 1.00 27.03
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                               73.914 41.987 13.865 1.00 26.60
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    ATOM
                               73.009 42.966 13.285 1.00 26.48
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                               72.786 42.717 11.781 1.00 26.52
            915 CB THR 275
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                                74.044 42.719 11.097 1.00 28.67
            916 OG1 THR 275
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                                71.919 43.799 11.198 1.00 27.35
            917 CG2 THR 275
    ATOM
            918 C THR 275
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    ATOM
            919 O THR 275
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                               69.970 44.069 15.276 1.00 24.61
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    ATOM
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                               70.057 44.987 16.506 1.00 23.61
            922 CB LEU 276
     ATOM
            923 CG LEU 276
                                71.199 44.730 17.503 1.00 24.36
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                                71.039 45.654 18.709 1.00 19.91
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            924 CD1 LEU 276
            925 CD2 LEU 276
                                71.225 43.253 17.947 1.00 22.20
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            926 C LEU 276
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    ATOM
                               69.100 45.556 13.623 1.00 25.35
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            927 O LEU 276
            928 N SER 277
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                               66.634 44.141 13.403 1.00 24.61
            929 CA SER 277
     ATOM
                               65.874 45.335 13.987 1.00 21.96
     ATOM
            930 CB SER 277
            931 OG SER 277
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            932 C SER 277
    ATOM
                               66.350 45.199 11.267 1.00 25.21
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            933 O SER 277
                               68.067 43.747 11.489 1.00 27.08
     ATOM
            934 N GLY 278
            935 CA GLY 278
                                68.556 43.899 10.127 1.00 29.27
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                               69.022 45.297 9.753 1.00 31.57
            936 C GLY 278
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            937 O GLY 278
                               69.303 45.564 8.591 1.00 31.42
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            938 N GLU 279
                               69.159 46.177 10.740 1.00 33.41
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                                69.558 47.560 10.484 1.00 34.84
            939 CA GLU 279
     ATOM
                                68.345 48.485 10.650 1.00 36.16
             940 CB GLU 279
     ATOM
            941 CG GLU 279
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                                66.566 49.419 12.206 1.00 41.07
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            942 CD GLU 279
            943 OE1 GLU 279
                                66.475 50.279 13.108 1.00 41.98
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                                65.643 49.197 11.399 1.00 43.80
            944 OE2 GLU 279
     ATOM
                               70.706 48.116 11.326 1.00 34.38
            945 C GLU 279
     ATOM
                               71.366 49.057 10.901 1.00 35.60
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             947 N MET 280
             948 CA MET 280
                                72.014 48.085 13.358 1.00 32.27
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                                71.443 48.544 14.702 1.00 31.81
             949 CB MET 280
     ATOM
     ATOM
             950 CG MET 280
                                72.471 49.181 15.637 1.00 29.76
             951 SD MET 280
                                71.813 49.482 17.289 1.00 29.63
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     ATOM
                                70.592 50.735 16.989 1.00 24.91
             952 CE MET 280
     ATOM
     ATOM
             953 C MET 280
                               73.161 47.119 13.603 1.00 32.51
                               72.995 46.117 14.303 1.00 32.78
             954 O MET 280
     ATOM
                               74.321 47.408 13.021 1.00 31.74
             955 N ALA 281
     ATOM
                               75.491 46.564 13.231 1.00 32.25
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     ATOM
             956 CA ALA 281
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                               76.261 48.202 14.805 1.00 34.06
            959 O ALA 281
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                               76.358 46.053 15.447 1.00 33.78
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            960 N VAL 282
                               76.913 46.366 16.755 1.00 33.45
            961 CA VAL 282
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    ATOM
            962 CB VAL 282
                               75.858 46.208 17.885 1.00 34.92
    ATOM
            963 CG1 VAL 282
                                74.775 47.269 17.744 1.00 34.90
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            964 CG2 VAL 282
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            965 C VAL 282
                               78.119 45.514 17.087 1.00 33.93
    ATOM
                               78.202 44.347 16.702 1.00 35.11
            966 O VAL 282
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    ATOM
                              79.071 46.123 17.777 1.00 33.49
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            967 N LYS 283
            968 CA LYS 283
                               80.285 45.446 18.187 1.00 34.83
    ATOM
            969 CB LYS 283
                               81.446 46.445 18.183 1.00 35.96
    ATOM
                               81.726 47.013 16.797 1.00 39.20
            970 CG LYS 283
    ATOM
                               82.621 48.245 16.844 1.00 43.38
    ATOM
            971 CD LYS 283
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            972 CE LYS 283
                               83.142 48.611 15.455 1.00 44.17
    ATOM
                               84.077 47.563 14.922 1.00 47.27
            973 NZ LYS 283
    ATOM
                              80.068 44.832 19.572 1.00 33.94
            974 C LYS 283
    ATOM
                              79.134 45.215 20.290 1.00 33.85
            975 O LYS 283
    ATOM
                               80.939 43.895 19.941 1.00 33.63
            976 N ARG 284
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    ATOM
                                80.873 43.184 21.217 1.00 34.00
    ATOM
            977 CA ARG 284
                                82.094 42.285 21.381 1.00 34.04
            978 CB ARG 284
    ATOM
                                82.332 41.369 20.219 1.00 36.31
            979 CG ARG 284
    ATOM
                                83.638 40.643 20.354 1.00 37.03
    ATOM
            980 CD ARG 284
            981 NE ARG 284
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    ATOM
                                83.323 38.326 19.583 1.00 40.07
            982 CZ ARG 284
    ATOM
                                82.804 37.973 20.759 1.00 39.78
    ATOM
            983 NH1 ARG 284
                                83.434 37.428 18.613 1.00 40.16
     ATOM
            984 NH2 ARG 284
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            985 C ARG 284
     ATOM
                               79.884 43.977 23.249 1.00 35.87
            986 O ARG 284
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                               81.763 44.993 22.530 1.00 35.75
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     ATOM
            988 CA GLU 285
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     ATOM
            990 CG GLU 285
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            991 CD GLU 285
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                                84.784 49.657 23.760 1.00 55.37
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     ATOM
            993 OE2 GLU 285
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            994 C GLU 285
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            995 O GLU 285
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            996 N GLN 286
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     ATOM
            997 CA GLN 286
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     ATOM
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                                79.632 49.497 20.500 1.00 35.09
     ATOM
            999 CG GLN 286
                                79.293 50.023 19.108 1.00 38.42
     ATOM 1000 CD GLN 286
                                 79.161 49.248 18.158 1.00 39.03
     ATOM 1001 OE1 GLN 286
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                                79.156 51.339 18.982 1.00 37.82
     ATOM 1002 NE2 GLN 286
     ATOM 1003 C GLN 286
                               77.605 47.308 22.970 1.00 29.57
                               76.870 47.891 23.770 1.00 26.96
     ATOM 1004 O GLN 286
                               77.352 46.080 22.524 1.00 29.50
     ATOM 1005 N LEU 287
     ATOM 1006 CA LEU 287
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75.831 44.182 22.029 1.00 27.14
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     ATOM 1008 CG LEU 287
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     ATOM 1009 CD1 LEU 287
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                                74.297 42.413 21.163 1.00 25.17
    ATOM 1010 CD2 LEU 287
     ATOM 1011 C LEU 287
                               76.303 44.874 24.433 1.00 28.10
     ATOM 1012 O LEU 287
                               75.301 44.748 25.155 1.00 28.58
                               77.541 44.652 24.868 1.00 27.97
     ATOM 1013 N LYS 288
                                77.808 44.218 26.230 1.00 28.55
     ATOM 1014 CA LYS 288
     ATOM 1015 CB LYS 288
                                79.270 43.800 26.376 1.00 28.93
                                79.603 43.254 27.750 1.00 32.46
    ATOM 1016 CG LYS 288
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                                81.015 42.725 27.826 1.00 33.48
     ATOM 1017 CD LYS 288
     ATOM 1018 CE LYS 288
                               81.205 41.878 29.071 1.00 35.76
     ATOM 1019 NZ LYS 288
                                82.525 41.186 29.029 1.00 40.52
                               77.497 45.341 27.220 1.00 29.15
     ATOM 1020 C LYS 288
                               76,782 45.132 28.207 1.00 31.28
     ATOM 1021 O LYS 288
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                               77.996 46.539 26.933 1.00 28.58
     ATOM 1022 N ASN 289
     ATOM 1023 CA ASN 289
                                77.794 47.692 27.811 1.00 28.40
     ATOM 1024 CB ASN 289
                                78.815 48.775 27.485 1.00 28.28
     ATOM 1025 CG ASN 289
                                80.224 48.329 27.770 1.00 31.30
     ATOM 1026 OD1 ASN 289
                                80.445 47.442 28.601 1.00 33.02
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     ATOM 1027 ND2 ASN 289
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     ATOM 1028 C ASN 289
                               76.395 48.278 27.792 1.00 28.33
                               76.005 48.977 28.724 1.00 28.36
     ATOM 1029 O ASN 289
     ATOM 1030 N GLY 290
                               75.638 47.977 26.740 1.00 26.71
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     ATOM 1031 CA GLY 290
                                74.286 48.487 26.606 1.00 23.27
     ATOM 1032 C GLY 290
                               73.233 47.852 27.484 1.00 22.93
                               72.063 48.219 27.399 1.00 23.84
     ATOM 1033 O GLY 290
     ATOM 1034 N GLY 291
                               73.620 46.905 28.330 1.00 21.30
     ATOM 1035 CA GLY 291
                               72.637 46.290 29.199 1.00 20.38
                               72.653 44.778 29.200 1.00 20.05
     ATOM 1036 C GLY 291
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     ATOM 1037 O GLY 291
                               72.190 44.165 30.147 1.00 21.91
     ATOM 1038 N LEU 292
                               73.211 44.173 28.160 1.00 21.36
     ATOM 1039 CA LEU 292
                                73.248 42.717 28.062 1.00 21.51
                                73.319 42.280 26.593 1.00 18.52
     ATOM 1040 CB LEU 292
     ATOM 1041 CG LEU 292
                                72.019 42.506 25.815 1.00 17.07
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     ATOM 1042 CD1 LEU 292
                                72.103 41.818 24.479 1.00 18.09
     ATOM 1043 CD2 LEU 292
                                70.844 41.947 26.599 1.00 16.35
     ATOM 1044 C LEU 292
                               74.347 42.046 28.872 1.00 22.17
                               74.176 40.923 29.352 1.00 21.91
     ATOM 1045 O LEU 292
     ATOM 1046 N GLY 293
                               75.479 42.724 29.011 1.00 23.76
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     ATOM 1047 CA GLY 293
                                76.588 42.169 29.760 1.00 23.92
     ATOM 1048 C GLY 293
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     ATOM 1049 O GLY 293
                               77.362 40.919 27.883 1.00 26.51
     ATOM 1050 N VAL 294
                               77.332 39.866 29.867 1.00 26.08
     ATOM 1051 CA VAL 294
                                77.854 38.618 29.329 1.00 26.34
45
                                78.263 37.636 30.443 1.00 26.97
     ATOM 1052 CB VAL 294
     ATOM 1053 CG1 VAL 294
                                79.440 38.199 31.209 1.00 28.20
     ATOM 1054 CG2 VAL 294
                               77.099 37.371 31.384 1.00 25.56
     ATOM 1055 C VAL 294
                               76.891 37.937 28.360 1.00 26.41
                               77.315 37.097 27.568 1.00 27.65
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     ATOM 1056 O VAL 294
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75.608 38.304 28.408 1.00 26.09
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    ATOM 1058 CA VAL 295
                                73.186 38.312 27.777 1.00 28.39
    ATOM 1059 CB VAL 295
                                 72.164 37.740 26.782 1.00 26.69
     ATOM 1060 CG1 VAL 295
     ATOM 1061 CG2 VAL 295
                                 72.763 38.005 29.206 1.00 26.23
    ATOM 1062 C VAL 295
                               75.035 38.089 26.069 1.00 25.83
                               74.903 37.286 25.151 1.00 27.12
    ATOM 1063 O VAL 295
    ATOM 1064 N SER 296
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    ATOM 1065 CA SER 296
                                76.097 39.725 24.619 1.00 26.17
    ATOM 1066 CB SER 296
                                76.665 41.132 24.742 1.00 25.82
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                                77.253 41.554 23.525 1.00 26.64
    ATOM 1067 OG SER 296
    ATOM 1068 C SER 296
                               77.196 38.783 24.142 1.00 28.63
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    ATOM 1069 O SER 296
                               78.118 38.443 25.046 1.00 29.69
    ATOM 1070 N ASP 297
                                79.211 37.531 24.731 1.00 28.96
    ATOM 1071 CA ASP 297
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                                80.058 37.234 25.973 1.00 31.82
    ATOM 1072 CB ASP 297
    ATOM 1073 CG ASP 297
                                80.768 38.454 26.506 1.00 35.23
                                80.958 39.429 25.743 1.00 35.71
    ATOM 1074 OD1 ASP 297
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     ATOM 1075 OD2 ASP 297
                               78.605 36.227 24.247 1.00 27.63
    ATOM 1076 C ASP 297
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    ATOM 1077 O ASP 297
                               79.048 35.666 23.248 1.00 29.88
    ATOM 1078 N ALA 298
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                                76.909 34.527 24.592 1.00 24.49
    ATOM 1079 CA ALA 298
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    ATOM 1080 CB ALA 298
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    ATOM 1081 C ALA 298
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    ATOM 1082 O ALA 298
                               76.589 33.654 22.357 1.00 24.83
    ATOM 1083 N ILE 299
                              75.632 35.647 22.814 1.00 24.70
    ATOM 1084 CA ILE 299
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    ATOM 1085 CB ILE 299
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                                73.338 36.876 20.005 1.00 19.17
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    ATOM 1086 CG2 ILE 299
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    ATOM 1087 CG1 ILE 299
    ATOM 1088 CD1 ILE 299
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                              76.127 35.829 20.428 1.00 22.33
    ATOM 1089 C ILE 299
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    ATOM 1090 O ILE 299
                               77.209 36.538 20.724 1.00 21.92
    ATOM 1091 N PHE 300
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    ATOM 1092 CA PHE 300
                                78.322 36.641 19.785 1.00 23.08
                                79.385 37.636 20.278 1.00 24.08
    ATOM 1093 CB PHE 300
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    ATOM 1094 CG PHE 300
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    ATOM 1095 CD1 PHE 300
                                79.857 39.331 18.471 1.00 23.76
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     ATOM 1096 CD2 PHE 300
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    ATOM 1097 CE1 PHE 300
    ATOM 1098 CE2 PHE 300
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    ATOM 1099 CZ PHE 300
                                78.957 41.558 18.554 1.00 22.46
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                               79.264 34.913 18.426 1.00 23.97
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    ATOM 1103 CA GLU 301
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    ATOM 1109 CB LEU 302
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                                73.953 31.120 18.979 1.00 22.61
    ATOM 1110 CG LEU 302
     ATOM 1111 CD1 LEU 302
                                74.084 29.612 19.193 1.00 22.31
                                72.611 31.604 19.485 1.00 19.27
     ATOM 1112 CD2 LEU 302
                               76.588 32.011 17.687 1.00 24.41
     ATOM 1113 C LEU 302
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    ATOM 1115 N GLY 303
                                76.746 33.816 16.062 1.00 25.87
     ATOM 1116 CA GLY 303
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                               77.975 33.288 15.338 1.00 28.63
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    ATOM 1118 O GLY 303
                               77.893 32.895 14.170 1.00 28.30
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     ATOM 1122 CG LYS 304
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     ATOM 1123 CD LYS 304
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     ATOM 1124 CE LYS 304
                                82.459 34.847 19.592 1.00 48.83
     ATOM 1125 NZ LYS 304
                               80.245 31.328 15.042 1.00 30.87
     ATOM 1126 C LYS 304
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                               80.632 30.944 13.932 1.00 29.53
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     ATOM 1129 CA SER 305
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     ATOM 1130 CB SER 305
     ATOM 1131 OG SER 305
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25
                               78.532 28.732 14.653 1.00 31.06
     ATOM 1132 C SER 305
                               78.745 27.799 13.872 1.00 31.84
     ATOM 1133 O SER 305
     ATOM 1134 N LEU 306
                               77.436 29.491 14.594 1.00 29.43
                                76.378 29.258 13.611 1.00 28.39
     ATOM 1135 CA LEU 306
                                75.121 30.055 13.962 1.00 26.05
     ATOM 1136 CB LEU 306
30
                                74.306 29.573 15.157 1.00 26.33
     ATOM 1137 CG LEU 306
                                73.061 30.430 15.285 1.00 26.22
     ATOM 1138 CD1 LEU 306
                                 73.924 28.110 14.985 1.00 25.86
     ATOM 1139 CD2 LEU 306
                               76.754 29.529 12.157 1.00 28.66
     ATOM 1140 C LEU 306
                               76.116 29.001 11.253 1.00 28.58
     ATOM 1141 O LEU 306
35
     ATOM 1142 N SER 307
                               77.786 30.338 11.931 1.00 29.72
                                78.224 30.667 10.577 1.00 31.19
     ATOM 1143 CA SER 307
                                79.466 31.556 10.617 1.00 30.15
     ATOM 1144 CB SER 307
     ATOM 1145 OG SER 307
                                79.226 32.710 11.396 1.00 35.19
     ATOM 1146 C SER 307
                               78.531 29.412 9.777 1.00 32.75
40
                               78.110 29.283 8.621 1.00 33.09
     ATOM 1147 O SER 307
                               79.248 28.482 10.407 1.00 33.36
     ATOM 1148 N ALA 308
     ATOM 1149 CA ALA 308
                                79.626 27.223 9.769 1.00 34.50
     ATOM 1150 CB ALA 308
                                80.636 26.473 10.637 1.00 33.55
     ATOM 1151 C ALA 308
                               78.417 26.328 9.466 1.00 35.00
45
                               78.469 25.501 8.550 1.00 37.10
     ATOM 1152 O ALA 308
                               77.335 26.496 10.226 1.00 32.76
     ATOM 1153 N PHE 309
     ATOM 1154 CA PHE 309
                                76.134 25.698 10.028 1.00 31.73
                                75.214 25.818 11.232 1.00 30.04
     ATOM 1155 CB PHE 309
     ATOM 1156 CG PHE 309
                                75.705 25.091 12.438 1.00 31.19
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ATOM 1157 CD1 PHE 309
                                74.973 24.048 12.975 1.00 31.61
    ATOM 1158 CD2 PHE 309
                                76.884 25.459 13.054 1.00 31.92
    ATOM 1159 CE1 PHE 309
                               75.400 23.391 14.110 1.00 31.22
    ATOM 1160 CE2 PHE 309
                               77.320 24.807 14.194 1.00 31.01
                               76.577 23.771 14.720 1.00 30.47
    ATOM 1161 CZ PHE 309
5
                              75.364 26.050 8.753 1.00 31.53
    ATOM 1162 C PHE 309
                              74.516 25.269 8.310 1.00 31.28
    ATOM 1163 O PHE 309
    ATOM 1164 N ASN 310
                               75.661 27.220 8.181 1.00 31.12
                               75.020 27.711 6.957 1.00 30.34
    ATOM 1165 CA ASN 310
    ATOM 1166 CB ASN 310
                               75.636 27.036 5.719 1.00 31.63
10
                               73.511 27.492 7.003 1.00 29.40
    ATOM 1167 C ASN 310
                               72.939 26.791 6.156 1.00 29.15
    ATOM 1168 O ASN 310
                               72.875 28.055 8.026 1.00 27.60
    ATOM 1169 N LEU 311
                               71.435 27.907 8.205 1.00 28.23
    ATOM 1170 CA LEU 311
                               71.021 28.313 9.621 1.00 27.41
    ATOM 1171 CB LEU 311
15
                               71.603 27.558 10.822 1.00 26.80
    ATOM 1172 CG LEU 311
    ATOM 1173 CD1 LEU 311
                                70.949 28.078 12.112 1.00 25.05
                              71.360 26.062 10.662 1.00 24.72
    ATOM 1174 CD2 LEU 311
                              70.628 28.719 7.192 1.00 29.01
    ATOM 1175 C LEU 311
    ATOM 1176 O LEU 311
                               71.040 29.808 6.782 1.00 30.66
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    ATOM 1177 N ASP 312
                              69.503 28.168 6.748 1.00 26.30
                               68.675 28.894 5.817 1.00 25.13
    ATOM 1178 CA ASP 312
                               68.391 28.067 4.539 1.00 23.90
    ATOM 1179 CB ASP 312
    ATOM 1180 CG ASP 312
                               67.438 26.890 4.754 1.00 21.34
                                66.959 26.631 5.868 1.00 22.47
    ATOM 1181 OD1 ASP 312
25
                                67.154 26.206 3.758 1.00 22.18
    ATOM 1182 OD2 ASP 312
                              67.419 29.379 6.542 1.00 24.49
    ATOM 1183 C ASP 312
    ATOM 1184 O ASP 312
                              67.221 29.056 7.725 1.00 24.01
    ATOM 1185 N ASP 313
                              66.587 30.153 5.845 1.00 23.40
                               65.363 30.697 6.421 1.00 22.63
    ATOM 1186 CA ASP 313
30
                               64.557 31.486 5.385 1.00 24.99
    ATOM 1187 CB ASP 313
    ATOM 1188 CG ASP 313
                               65.224 32.799 4.994 1.00 28.02
                                66.036 33.334 5.778 1.00 30.34
    ATOM 1189 OD1 ASP 313
                                64.936 33.306 3.897 1.00 30.41
    ATOM 1190 OD2 ASP 313
                              64.480 29.650 7.053 1.00 21.47
    ATOM 1191 C ASP 313
35
    ATOM 1192 O ASP 313
                              63.853 29.917 8.082 1.00 21.76
                               64.407 28.474 6.435 1.00 19.16
    ATOM 1193 N THR 314
                               63.580 27.386 6.966 1.00 18.79
    ATOM 1194 CA THR 314
                               63.398 26.240 5.913 1.00 19.68
    ATOM 1195 CB THR 314
                                62.743 26.758 4.747 1.00 20.56
40
    ATOM 1196 OG1 THR 314
                                62.558 25.112 6.482 1.00 18.84
     ATOM 1197 CG2 THR 314
                               64.133 26.818 8.293 1.00 15.38
     ATOM 1198 C THR 314
    ATOM 1199 O THR 314
                               63.383 26.538 9.223 1.00 14.08
     ATOM 1200 N GLU 315
                               65.445 26.656 8.376 1.00 15.16
                                66.051 26.126 9.593 1.00 16.78
     ATOM 1201 CA GLU 315
45
     ATOM 1202 CB GLU 315
                                67.513 25.785 9.340 1.00 14.29
     ATOM 1203 CG GLU 315
                                67.611 24.483 8.579 1.00 15.13
                                68.910 24.291 7.872 1.00 15.90
     ATOM 1204 CD GLU 315
    ATOM 1205 OE1 GLU 315
                               69.625 25.285 7.639 1.00 19.80
     ATOM 1206 OE2 GLU 315
                                69.211 23.129 7.527 1.00 19.34
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65.872 27.119 10.736 1.00 17.27
    ATOM 1207 C GLU 315
                               65.457 26.742 11.836 1.00 17.46
    ATOM 1208 O GLU 315
                               66.081 28.399 10.440 1.00 17.12
    ATOM 1209 N VAL 316
                                65.897 29.441 11.446 1.00 16.92
    ATOM 1210 CA VAL 316
    ATOM 1211 CB VAL 316
                                66.336 30.828 10.918 1.00 15.89
                                66.062 31.921 11.962 1.00 14.60
    ATOM 1212 CG1 VAL 316
                                67.811 30.785 10.579 1.00 15.95
    ATOM 1213 CG2 VAL 316
                               64.430 29.472 11.869 1.00 17.32
    ATOM 1214 C VAL 316
                               64.131 29.582 13.055 1.00 18.11
    ATOM 1215 O VAL 316
                               63.515 29.324 10.905 1.00 17.42
    ATOM 1216 N ALA 317
10
                               62.076 29.342 11.195 1.00 16.21
    ATOM 1217 CA ALA 317
                                61.262 29.321 9.910 1.00 14.63
    ATOM 1218 CB ALA 317
                               61.656 28.181 12.079 1.00 16.84
    ATOM 1219 C ALA 317
                               60.904 28.359 13.036 1.00 16.08
    ATOM 1220 O ALA 317
                               62.146 26.990 11.759 1.00 17.27
    ATOM 1221 N LEU 318
15
     ATOM 1222 CA LEU 318
                               61.783 25.804 12.526 1.00 17.88
                                62.141 24.525 11.748 1.00 17.58
     ATOM 1223 CB LEU 318
                                61.331 24.333 10.439 1.00 16.87
     ATOM 1224 CG LEU 318
                                61.837 23.155 9.658 1.00 15.79
     ATOM 1225 CD1 LEU 318
                                59.860 24.149 10.728 1.00 14.08
     ATOM 1226 CD2 LEU 318
20
                               62.394 25.852 13.932 1.00 18.20
     ATOM 1227 C LEU 318
                               61.733 25.495 14.910 1.00 18.71
     ATOM 1228 O LEU 318
                               63.614 26.380 14.034 1.00 17.73
     ATOM 1229 N LEU 319
                               64.288 26.531 15.321 1.00 16.57
     ATOM 1230 CA LEU 319
                                65.689 27.105 15.107 1.00 18.81
     ATOM 1231 CB LEU 319
25
                                66.733 27.223 16.224 1.00 21.77
     ATOM 1232 CG LEU 319
                                66.767 25.994 17.117 1.00 23.03
     ATOM 1233 CD1 LEU 319
                                68.076 27.421 15.554 1.00 20.86
     ATOM 1234 CD2 LEU 319
                               63.433 27.471 16.160 1.00 16.07
     ATOM 1235 C LEU 319
                               63.134 27.183 17.319 1.00 16.40
     ATOM 1236 O LEU 319
30
                               62.948 28.546 15.545 1.00 13.91
     ATOM 1237 N GLN 320
                                62.101 29.490 16.253 1.00 13.86
     ATOM 1238 CA GLN 320
                                61.782 30.697 15.373 1.00 13.26
     ATOM 1239 CB GLN 320
                                62.994 31.553 15.080 1.00 12.17
     ATOM 1240 CG GLN 320
                                62.691 32.802 14.253 1.00 13.98
     ATOM 1241 CD GLN 320
35
                                63.597 33.568 13.950 1.00 15.61
     ATOM 1242 OE1 GLN 320
                                61.436 32.993 13.862 1.00 13.85
     ATOM 1243 NE2 GLN 320
                               60.813 28.832 16.746 1.00 14.52
     ATOM 1244 C GLN 320
                               60.367 29.087 17.864 1.00 15.12
     ATOM 1245 O GLN 320
                               60.211 27.982 15.924 1.00 14.21
     ATOM 1246 N ALA 321
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                                58.976 27.298 16.309 1.00 15.04
     ATOM 1247 CA ALA 321
                                58.408 26.519 15.115 1.00 13.84
     ATOM 1248 CB ALA 321
                               59.217 26.349 17.487 1.00 15.98
     ATOM 1249 C ALA 321
     ATOM 1250 O ALA 321
                               58.358 26.197 18.355 1.00 15.12
                               60.373 25.687 17.488 1.00 16.63
     ATOM 1251 N VAL 322
45
                                60.720 24.757 18.557 1.00 18.74
     ATOM 1252 CA VAL 322
                                62.012 23.943 18.231 1.00 19.42
     ATOM 1253 CB VAL 322
                                62.493 23.154 19.455 1.00 19.45
     ATOM 1254 CG1 VAL 322
                                61.745 22.986 17.083 1.00 19.05
     ATOM 1255 CG2 VAL 322
     ATOM 1256 C VAL 322
                               60.910 25.556 19.833 1.00 18.42
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60.421 25.164 20.886 1.00 19.46
     ATOM 1257 O VAL 322
                               61.607 26.685 19.735 1.00 18.65
     ATOM 1258 N LEU 323
                                61.836 27.543 20.894 1.00 18.49
     ATOM 1259 CA LEU 323
                                62.710 28.740 20.508 1.00 18.36
    ATOM 1260 CB LEU 323
                                64.179 28.449 20.186 1.00 18.13
     ATOM 1261 CG LEU 323
                                64.829 29.669 19.585 1.00 17.37
     ATOM 1262 CD1 LEU 323
                                64.923 27.999 21.447 1.00 17.27
     ATOM 1263 CD2 LEU 323
                               60.499 28.029 21.454 1.00 18.38
     ATOM 1264 C LEU 323
    ATOM 1265 O LEU 323
                               60.275 28.008 22.663 1.00 18.81
    ATOM 1266 N LEU 324
                               59.595 28.406 20.557 1.00 18.67
10
                                58.275 28.897 20.924 1.00 19.02
     ATOM 1267 CA LEU 324
                                57.564 29.467 19.685 1.00 17.78
     ATOM 1268 CB LEU 324
     ATOM 1269 CG LEU 324
                                56.095 29.891 19.838 1.00 17.59
     ATOM 1270 CD1 LEU 324
                                55.983 31.123 20.709 1.00 18.15
                                55.489 30.180 18.476 1.00 16.43
     ATOM 1271 CD2 LEU 324
15
     ATOM 1272 C LEU 324
                               57.354 27.884 21.610 1.00 19.62
                               56.735 28.185 22.633 1.00 19.40
     ATOM 1273 O LEU 324
                               57.224 26.701 21.029 1.00 21.14
     ATOM 1274 N MET 325
     ATOM 1275 CA MET 325
                                56.330 25.680 21.585 1.00 24.06
     ATOM 1276 CB MET 325
                                55.857 24.738 20.473 1.00 24.68
20
                                55.169 25.444 19.303 1.00 24.49
     ATOM 1277 CG MET 325
     ATOM 1278 SD MET 325
                                53.759 26.457 19.820 1.00 26.18
     ATOM 1279 CE MET 325
                                52.609 25.252 20.373 1.00 24.03
                               56.996 24.887 22.705 1.00 26.15
     ATOM 1280 C MET 325
                               57.021 23.664 22.693 1.00 25.68
25
     ATOM 1281 O MET 325
                               57.555 25.593 23.671 1.00 29.34
     ATOM 1282 N SER 326
                                58.232 24.938 24.774 1.00 32.40
     ATOM 1283 CA SER 326
                                59.512 25.701 25.112 1.00 32.12
     ATOM 1284 CB SER 326
                                60.127 25.173 26.272 1.00 36.86
     ATOM 1285 OG SER 326
                               57.317 24.831 25.996 1.00 34.04
     ATOM 1286 C SER 326
30
                               56.532 25.741 26.280 1.00 33.24
     ATOM 1287 O SER 326
                               57.366 23.687 26.674 1.00 35.62
     ATOM 1288 N THR 327
                                56.560 23.486 27.867 1.00 36.88
     ATOM 1289 CA THR 327
     ATOM 1290 CB THR 327
                                55.938 22.085 27.907 1.00 36.58
                                 56.953 21.094 27.714 1.00 38.58
     ATOM 1291 OG1 THR 327
35
                                 54.883 21.938 26.826 1.00 37.73
     ATOM 1292 CG2 THR 327
                               57.378 23.733 29.135 1.00 38.77
     ATOM 1293 C THR 327
                               56.921 23.438 30.240 1.00 39.53
     ATOM 1294 O THR 327
                               58.593 24.260 28.972 1.00 41.25
     ATOM 1295 N ASP 328
                                59.473 24.573 30.099 1.00 43.20
     ATOM 1296 CA ASP 328
40
     ATOM 1297 CB ASP 328
                                60.940 24.698 29.655 1.00 46.47
     ATOM 1298 CG ASP 328
                                61.618 23.346 29.439 1.00 51.94
                                62.547 23.278 28.601 1.00 55.43
     ATOM 1299 OD1 ASP 328
     ATOM 1300 OD2 ASP 328
                                61.251 22.354 30.111 1.00 54.77
45
     ATOM 1301 C ASP 328
                               59.001 25.905 30.653 1.00 43.79
                               59.755 26.877 30.709 1.00 45.91
     ATOM 1302 O ASP 328
     ATOM 1303 N ARG 329
                               57.724 25.967 30.995 1.00 43.55
     ATOM 1304 CA ARG 329
                                57.143 27.178 31.542 1.00 43.04
     ATOM 1305 CB ARG 329
                                56.398 27.997 30.482 1.00 43.87
                                57.258 28.740 29.504 1.00 40.87
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     ATOM 1306 CG ARG 329
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57.545 27.886 28.314 1.00 39.52
     ATOM 1307 CD ARG 329
     ATOM 1308 NE ARG 329
                                58.301 28.643 27.341 1.00 38.90
     ATOM 1309 CZ ARG 329
                                59.624 28.708 27.313 1.00 40.59
                                60.359 28.052 28.196 1.00 42.41
     ATOM 1310 NH1 ARG 329
                                60.210 29.466 26.413 1.00 41.87
     ATOM 1311 NH2 ARG 329
 5
                               56.152 26.817 32.609 1.00 43.00
     ATOM 1312 C ARG 329
     ATOM 1313 O ARG 329
                               55.600 25.716 32.628 1.00 43.66
                               55.886 27.797 33.456 1.00 41.58
     ATOM 1314 N SER 330
                               54.953 27.641 34.538 1.00 40.11
     ATOM 1315 CA SER 330
     ATOM 1316 CB SER 330
                              55.491 28.362 35.777 1.00 40.38
10
     ATOM 1317 C SER 330
                               53.602 28.223 34.103 1.00 38.99
                               53.553 29.172 33.320 1.00 39.22
     ATOM 1318 O SER 330
                               52.517 27.581 34.529 1.00 37.52
     ATOM 1319 N GLY 331
                               51.176 28.063 34.232 1.00 35.64
     ATOM 1320 CA GLY 331
                               50.493 27.782 32.906 1.00 35.14
     ATOM 1321 C GLY 331
15
                               49.439 28.363 32.640 1.00 34.48
     ATOM 1322 O GLY 331
                               51.059 26.925 32.066 1.00 34.54
     ATOM 1323 N LEU 332
     ATOM 1324 CA LEU 332
                                50.424 26.637 30.780 1.00 34.59
     ATOM 1325 CB LEU 332
                                51.394 25.942 29.828 1.00 33.09
     ATOM 1326 CG LEU 332
                                52.532 26.765 29.236 1.00 32.72
20
                                53.473 25.834 28.497 1.00 30.29
     ATOM 1327 CD1 LEU 332
     ATOM 1328 CD2 LEU 332
                                51.987 27.844 28.313 1.00 29.20
     ATOM 1329 C LEU 332
                               49.191 25.763 30.969 1.00 35.14
                               49.178 24.874 31.811 1.00 35.96
     ATOM 1330 O LEU 332
                               48.153 26.076 30.204 1.00 35.65
25
     ATOM 1331 N LEU 333
                                46.898 25.345 30.215 1.00 37.97
     ATOM 1332 CA LEU 333
                               45.743 26.271 29.796 1.00 40.71
     ATOM 1333 CB LEU 333
                                45.389 27.483 30.670 1.00 43.46
     ATOM 1334 CG LEU 333
     ATOM 1335 CD1 LEU 333
                                44.713 28.620 29.882 1.00 42.72
                                44.487 27.021 31.806 1.00 45.25
     ATOM 1336 CD2 LEU 333
30
                               46.952 24.115 29.300 1.00 37.78
     ATOM 1337 C LEU 333
     ATOM 1338 O LEU 333
                               46.695 22.991 29.720 1.00 37.65
                               47.361 24.323 28.060 1.00 38.65
     ATOM 1339 N CYA 334
     ATOM 1340 CA CYA 334
                                47.413 23.249 27.073 1.00 40.91
     ATOM 1341 CB CYA 334
                                46.936 23.788 25.721 1.00 47.35
35
                                45.406 24.693 25.867 1.00 52.24
     ATOM 1342 SG CYA 334
     ATOM 1343 AS CYA 334
                                44.066 22.890 25.562 1.00 70.72
                               48.778 22.588 26.901 1.00 39.85
     ATOM 1344 C CYA 334
     ATOM 1345 O CYA 334
                               49.287 22.473 25.775 1.00 39.54
     ATOM 1346 N VAL 335
                               49.329 22.078 27.997 1.00 37.67
40
     ATOM 1347 CA VAL 335
                                50.641 21.432 27.967 1.00 36.07
     ATOM 1348 CB VAL 335
                                51.019 20.905 29.384 1.00 33.70
                                 52.434 20.332 29.401 1.00 33.70
     ATOM 1349 CG1 VAL 335
                                 50.913 22.028 30.387 1.00 31.84
     ATOM 1350 CG2 VAL 335
45
     ATOM 1351 C VAL 335
                               50.734 20.334 26.885 1.00 36.09
                               51.662 20.335 26.064 1.00 34.41
     ATOM 1352 O VAL 335
                               49.747 19.444 26.833 1.00 35.95
     ATOM 1353 N ASP 336
     ATOM 1354 CA ASP 336
                              49.748 18.372 25.844 1.00 36.34
                               48.591 17.394 26.091 1.00 41.36
     ATOM 1355 CB ASP 336
     ATOM 1356 CG ASP 336 48.613 16.206 25.129 1.00 46.23
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ATOM 1357 OD1 ASP 336
                                47.615 16.021 24.392 1.00 49.55
                                49.639 15.470 25.097 1.00 48.07
     ATOM 1358 OD2 ASP 336
                               49.727 18.846 24.390 1.00 33.05
    ATOM 1359 C ASP 336
                               50.527 18.377 23.573 1.00 32.33
    ATOM 1360 O ASP 336
    ATOM 1361 N LYS 337
                               48.794 19.743 24.076 1.00 29.57
5
                               48.661 20.286 22.723 1.00 27.76
    ATOM 1362 CA LYS 337
                               47.520 21.313 22.689 1.00 27.09
     ATOM 1363 CB LYS 337
                               49.988 20.941 22.286 1.00 27.64
    ATOM 1364 C LYS 337
                               50.472 20.713 21.173 1.00 26.09
    ATOM 1365 O LYS 337
                              50.597 21.688 23.208 1.00 25.90
    ATOM 1366 N ILE 338
10
     ATOM 1367 CA ILE 338
                               51.852 22.394 22.971 1.00 24.21
                               52.128 23.391 24.122 1.00 23.30
     ATOM 1368 CB ILE 338
                               53.500 24.048 23.958 1.00 21.75
     ATOM 1369 CG2 ILE 338
                               51.014 24.448 24.155 1.00 21.19
     ATOM 1370 CG1 ILE 338
                               51.055 25.393 25.361 1.00 21.39
     ATOM 1371 CD1 ILE 338
15
                              53.041 21.451 22.782 1.00 25.55
     ATOM 1372 C ILE 338
                              53.861 21.640 21.875 1.00 24.74
     ATOM 1373 O ILE 338
     ATOM 1374 N GLU 339
                               53.124 20.421 23.622 1.00 27.43
                                54.220 19.448 23.536 1.00 27.60
     ATOM 1375 CA GLU 339
                                54.201 18.512 24.755 1.00 27.21
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     ATOM 1376 CB GLU 339
                               54.112 18.650 22.236 1.00 26.85
     ATOM 1377 C GLU 339
                               55.119 18.385 21.581 1.00 26.71
     ATOM 1378 O GLU 339
                               52.888 18.276 21.872 1.00 27.04
     ATOM 1379 N LYS 340
     ATOM 1380 CA LYS 340
                               52.663 17.515 20.654 1.00 28.19
     ATOM 1381 CB LYS 340
                               51.210 17.008 20.609 1.00 28.67
25
                               53.002 18.402 19.439 1.00 27.96
     ATOM 1382 C LYS 340
                               53.558 17.934 18.436 1.00 27.48
     ATOM 1383 O LYS 340
                               52.746 19.700 19.567 1.00 28.32
     ATOM 1384 N SER 341
                              53.058 20.662 18.514 1.00 28.02
     ATOM 1385 CA SER 341
                               52.457 22.022 18.867 1.00 31.25
30
     ATOM 1386 CB SER 341
                               52.880 23.029 17.965 1.00 37.69
     ATOM 1387 OG SER 341
                               54.578 20.773 18.350 1.00 26.01
     ATOM 1388 C SER 341
                               55.096 20.717 17.234 1.00 25.06
     ATOM 1389 O SER 341
                               55.297 20.899 19.462 1.00 25.71
     ATOM 1390 N GLN 342
     ATOM 1391 CA GLN 342
                               56.750 20.993 19.398 1.00 26.39
35
                                57.356 21.254 20.777 1.00 24.17
     ATOM 1392 CB GLN 342
                                58.834 21.590 20.703 1.00 25.09
     ATOM 1393 CG GLN 342
                                59.476 21.677 22.057 1.00 26.93
     ATOM 1394 CD GLN 342
     ATOM 1395 OE1 GLN 342
                                59.479 20.704 22.810 1.00 27.77
     ATOM 1396 NE2 GLN 342
                                60.022 22.839 22.386 1.00 24.61
40
     ATOM 1397 C GLN 342
                               57.354 19.715 18.806 1.00 25.69
                               58.356 19.771 18.075 1.00 24.99
     ATOM 1398 O GLN 342
                               56.753 18.569 19.127 1.00 25.00
     ATOM 1399 N GLU 343
                                57.222 17.280 18.610 1.00 25.34
     ATOM 1400 CA GLU 343
                                56.411 16.118 19.245 1.00 25.90
45
     ATOM 1401 CB GLU 343
                               57.089 17.276 17.076 1.00 24.32
     ATOM 1402 C GLU 343
                               58.021 16.891 16.365 1.00 23.99
     ATOM 1403 O GLU 343
                               55.961 17.789 16.587 1.00 23.56
     ATOM 1404 N ALA 344
     ATOM 1405 CA ALA 344 55.701 17.875 15.153 1.00 22.85
                                54.320 18.451 14.917 1.00 22.64
     ATOM 1406 CB ALA 344
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ATOM 1407 C ALA 344
                               56.768 18.743 14.489 1.00 22.77
                               57.355 18.360 13.477 1.00 22.08
    ATOM 1408 O ALA 344
                               57.057 19.893 15.092 1.00 21.89
    ATOM 1409 N TYR 345
                                58.075 20.792 14.550 1.00 21.18
    ATOM 1410 CA TYR 345
                                58.108 22.119 15.313 1.00 20.27
5
    ATOM 1411 CB TYR 345
                                57.048 23.078 14.856 1.00 17.45
    ATOM 1412 CG TYR 345
                                56.001 23.431 15.698 1.00 17.99
    ATOM 1413 CD1 TYR 345
    ATOM 1414 CE1 TYR 345
                                54.992 24.253 15.270 1.00 19.97
    ATOM 1415 CD2 TYR 345
                                57.063 23.589 13.562 1.00 19.11
                                56.055 24.424 13.116 1.00 19.14
    ATOM 1416 CE2 TYR 345
10
                                55.017 24.749 13.972 1.00 20.78
    ATOM 1417 CZ TYR 345
                                53.983 25.539 13.530 1.00 20.70
    ATOM 1418 OH TYR 345
    ATOM 1419 C TYR 345
                               59.454 20.167 14.583 1.00 20.96
                               60.221 20.314 13.632 1.00 22.29
    ATOM 1420 O TYR 345
                               59.778 19.480 15.677 1.00 20.82
    ATOM 1421 N LEU 346
15
                                61.079 18.838 15.817 1.00 20.18
    ATOM 1422 CA LEU 346
                                61.216 18.203 17.205 1.00 21.04
    ATOM 1423 CB LEU 346
    ATOM 1424 CG LEU 346
                                61.606 19.158 18.335 1.00 21.25
                                61.226 18.595 19.685 1.00 20.95
    ATOM 1425 CD1 LEU 346
                                63.099 19.438 18.267 1.00 19.90
    ATOM 1426 CD2 LEU 346
20
                               61.317 17.806 14.716 1.00 20.19
    ATOM 1427 C LEU 346
    ATOM 1428 O LEU 346
                               62.407 17.755 14.142 1.00 20.69
                               60.290 17.016 14.390 1.00 22.00
    ATOM 1429 N LEU 347
    ATOM 1430 CA LEU 347
                                60.406 15.994 13.344 1.00 21.81
    ATOM 1431 CB LEU 347
                                59.199 15.051 13.366 1.00 24.03
25
                                59.301 13.805 14.250 1.00 26.28
    ATOM 1432 CG LEU 347
                                57.964 13.072 14.277 1.00 27.79
    ATOM 1433 CD1 LEU 347
                                60.409 12.889 13.728 1.00 24.78
     ATOM 1434 CD2 LEU 347
     ATOM 1435 C LEU 347
                               60.544 16.623 11.966 1.00 20.50
                               61.351 16.179 11.143 1.00 21.39
     ATOM 1436 O LEU 347
30
    ATOM 1437 N ALA 348
                               59.767 17.674 11.727 1.00 20.84
                                59.788 18.381 10.456 1.00 18.12
     ATOM 1438 CA ALA 348
                                58.729 19.480 10.457 1.00 18.49
     ATOM 1439 CB ALA 348
                               61.168 18.963 10.269 1.00 17.53
     ATOM 1440 C ALA 348
                               61.785 18.781 9.228 1.00 18.78
     ATOM 1441 O ALA 348
35
                               61.677 19.569 11.338 1.00 19.55
     ATOM 1442 N PHE 349
                                63.001 20.196 11.389 1.00 19.84
     ATOM 1443 CA PHE 349
     ATOM 1444 CB PHE 349
                                63.188 20.823 12.786 1.00 18.68
     ATOM 1445 CG PHE 349
                                64.380 21.758 12.917 1.00 19.12
                                65.234 22.008 11.851 1.00 19.95
     ATOM 1446 CD1 PHE 349
40
     ATOM 1447 CD2 PHE 349
                                64.618 22.420 14.126 1.00 20.06
                                66.294 22.905 11.971 1.00 18.99
     ATOM 1448 CE1 PHE 349
     ATOM 1449 CE2 PHE 349
                                65.674 23.317 14.261 1.00 16.79
     ATOM 1450 CZ PHE 349
                                66.516 23.562 13.184 1.00 18.91
                               64.108 19.170 11.103 1.00 20.44
     ATOM 1451 C PHE 349
45
                               64.980 19.401 10.260 1.00 19.83
     ATOM 1452 O PHE 349
     ATOM 1453 N GLU 350
                               64.064 18.032 11.794 1.00 23.59
     ATOM 1454 CA GLU 350
                                65.077 16.995 11.610 1.00 23.46
                                64.830 15.845 12.584 1.00 25.26
     ATOM 1455 CB GLU 350
     ATOM 1456 CG GLU 350
                                65.694 14.644 12.288 1.00 31.98
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65.526 13.482 13.257 1.00 35.49
     ATOM 1457 CD GLU 350
                                66.560 12.853 13.555 1.00 40.26
     ATOM 1458 OE1 GLU 350
     ATOM 1459 OE2 GLU 350
                                64.380 13.173 13.689 1.00 36.23
     ATOM 1460 C GLU 350
                               65.083 16.489 10.165 1.00 21.12
                               66.133 16.384 9.526 1.00 19.81
     ATOM 1461 O GLU 350
     ATOM 1462 N HIS 351
                              63.888 16.234 9.651 1.00 21.98
                               63.694 15.751 8.292 1.00 21.31
     ATOM 1463 CA HIS 351
     ATOM 1464 CB HIS 351
                               62.238 15.321 8.107 1.00 21.76
     ATOM 1465 CG HIS 351
                               61.839 14.160 8.967 1.00 22.08
                               62.578 13.317 9.728 1.00 22.65
10
     ATOM 1466 CD2 HIS 351
     ATOM 1467 ND1 HIS 351
                                60.532 13.751 9.115 1.00 22.37
                               60.478 12.716 9.930 1.00 21.44
     ATOM 1468 CE1 HIS 351
                               61.705 12.429 10.314 1.00 20.85
     ATOM 1469 NE2 HIS 351
                              64.117 16.815 7.275 1.00 21.18
     ATOM 1470 C HIS 351
     ATOM 1471 O HIS 351
                              64.683 16.489 6.231 1.00 22.65
15
     ATOM 1472 N TYR 352
                               63.915 18.088 7.602 1.00 19.79
     ATOM 1473 CA TYR 352
                                64.327 19.146 6.697 1.00 18.72
                                63.768 20.502 7.122 1.00 19.55
     ATOM 1474 CB TYR 352
     ATOM 1475 CG TYR 352
                                64.140 21.580 6.137 1.00 19.27
     ATOM 1476 CD1 TYR 352
                                63.556 21.623 4.867 1.00 19.29
20
                                63.961 22.555 3.927 1.00 17.55
     ATOM 1477 CE1 TYR 352
                                65.132 22.507 6.438 1.00 18.91
     ATOM 1478 CD2 TYR 352
     ATOM 1479 CE2 TYR 352
                                65.545 23.443 5.503 1.00 17.30
                                64.954 23.459 4.256 1.00 18.41
     ATOM 1480 CZ TYR 352
                                65.355 24.384 3.334 1.00 19.40
25
     ATOM 1481 OH TYR 352
                               65.849 19.182 6.687 1.00 19.31
     ATOM 1482 C TYR 352
                               66.479 19.333 5.639 1.00 20.25
     ATOM 1483 O TYR 352
                               66.446 19.017 7.858 1.00 21.25
     ATOM 1484 N VAL 353
     ATOM 1485 CA VAL 353
                                67.899 18.993 7.960 1.00 22.03
                                68.348 18.880 9.450 1.00 22.60
     ATOM 1486 CB VAL 353
30
     ATOM 1487 CG1 VAL 353
                                69.843 18.635 9.550 1.00 20.34
     ATOM 1488 CG2 VAL 353
                                67.997 20.167 10.183 1.00 22.61
                               68.442 17.827 7.108 1.00 22.74
     ATOM 1489 C VAL 353
     ATOM 1490 O VAL 353
                               69.448 17.985 6.398 1.00 23.44
                               67.773 16.674 7.165 1.00 22.30
35
     ATOM 1491 N ASN 354
                                68.185 15.508 6.373 1.00 23.56
     ATOM 1492 CA ASN 354
     ATOM 1493 CB ASN 354
                                67.241 14.320 6.603 1.00 22.26
                                67.374 13.715 7.981 1.00 23.06
     ATOM 1494 CG ASN 354
                                 68.406 13.843 8.628 1.00 25.79
     ATOM 1495 OD1 ASN 354
                                 66.327 13.044 8.435 1.00 21.07
     ATOM 1496 ND2 ASN 354
40
     ATOM 1497 C ASN 354
                               68.134 15.877 4.888 1.00 25.10
     ATOM 1498 O ASN 354
                               69.024 15.534 4.111 1.00 26.70
                              67.067 16.568 4.503 1.00 24.50
     ATOM 1499 N HIS 355
                               66.881 16.986 3.123 1.00 24.46
     ATOM 1500 CA HIS 355
45
     ATOM 1501 CB HIS 355
                               65.557 17.750 2.969 1.00 26.07
                               65.365 18.337 1.604 1.00 28.28
     ATOM 1502 CG HIS 355
                               65.918 19.422 1.018 1.00 28.10
     ATOM 1503 CD2 HIS 355
     ATOM 1504 ND1 HIS 355
                                64.600 17.724 0.632 1.00 26.32
                               64.706 18.407 -0.499 1.00 27.71
     ATOM 1505 CE1 HIS 355
                               65.502 19.435 -0.288 1.00 27.79
50
     ATOM 1506 NE2 HIS 355
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68.022 17.857 2.624 1.00 24.07
    ATOM 1507 C HIS 355
    ATOM 1508 O HIS 355
                              68.460 17.729 1.484 1.00 23.54
                               68.463 18.774 3.471 1.00 25.31
    ATOM 1509 N ARG 356
                                69.523 19.714 3.130 1.00 25.69
    ATOM 1510 CA ARG 356
                                69.561 20.820 4.168 1.00 24.06
 5
    ATOM 1511 CB ARG 356
                                68.337 21.682 4.094 1.00 23.23
    ATOM 1512 CG ARG 356
    ATOM 1513 CD ARG 356
                                68.670 22.973 3.424 1.00 25.91
                                69.447 23.814 4.322 1.00 24.87
    ATOM 1514 NE ARG 356
                                70.325 24.726 3.928 1.00 25.05
    ATOM 1515 CZ ARG 356
    ATOM 1516 NH1 ARG 356
                                70.546 24.920 2.640 1.00 24.97
10
    ATOM 1517 NH2 ARG 356
                                70.978 25.453 4.831 1.00 25.62
                               70.900 19.109 2.949 1.00 27.73
    ATOM 1518 C ARG 356
                               71.724 19.645 2.208 1.00 28.38
    ATOM 1519 O ARG 356
                               71.179 18.048 3.693 1.00 29.45
    ATOM 1520 N LYS 357
                               72.457 17.355 3.588 1.00 31.35
    ATOM 1521 CA LYS 357
15
    ATOM 1522 CB LYS 357
                               72.503 16.566 2.270 1.00 32.80
                               71.290 15.650 2.103 1.00 35.78
    ATOM 1523 CG LYS 357
    ATOM 1524 CD LYS 357
                               71.264 14.927 0.778 1.00 39.43
    ATOM 1525 CE LYS 357
                               70.121 13.918 0.739 1.00 42.93
                               70.162 13.074 -0.498 1.00 45.97
    ATOM 1526 NZ LYS 357
20
                               73.692 18.247 3.743 1.00 31.34
    ATOM 1527 C LYS 357
    ATOM 1528 O LYS 357
                               74.489 18.390 2.818 1.00 32.65
    ATOM 1529 N HIS 358
                              73.837 18.861 4.913 1.00 30.72
                               74.995 19.706 5.186 1.00 31.49
    ATOM 1530 CA HIS 358
                               74.895 20.322 6.579 1.00 29.13
25
    ATOM 1531 CB HIS 358
                               73.882 21.415 6.688 1.00 25.30
    ATOM 1532 CG HIS 358
                               74.026 22.760 6.646 1.00 24.90
    ATOM 1533 CD2 HIS 358
                               72.543 21.175 6.892 1.00 24.54
    ATOM 1534 ND1 HIS 358
                               71.901 22.324 6.975 1.00 23.68
    ATOM 1535 CE1 HIS 358
                               72.777 23.302 6.830 1.00 25.28
    ATOM 1536 NE2 HIS 358
30
    ATOM 1537 C HIS 358
                              76.235 18.831 5.161 1.00 33.38
                              76.166 17.647 5.495 1.00 35.46
    ATOM 1538 O HIS 358
                               77.366 19.399 4.768 1.00 35.34
    ATOM 1539 N ASN 359
    ATOM 1540 CA ASN 359
                                78.606 18.636 4.746 1.00 38.17
                                79.544 19.150 3.646 1.00 37.84
    ATOM 1541 CB ASN 359
35
                               79.236 18.825 6.120 1.00 39.85
    ATOM 1542 C ASN 359
    ATOM 1543 O ASN 359
                               80.317 19.406 6.240 1.00 42.72
                              78.510 18.411 7.159 1.00 39.01
    ATOM 1544 N ILE 360
    ATOM 1545 CA ILE 360
                               78.968 18.526 8.549 1.00 36.72
                               78.351 19.752 9.264 1.00 37.69
    ATOM 1546 CB ILE 360
40
     ATOM 1547 CG2 ILE 360
                               78.802 19.793 10.722 1.00 37.56
     ATOM 1548 CG1 ILE 360
                               78.735 21.049 8.549 1.00 37.68
                               77.970 22.253 9.041 1.00 38.40
     ATOM 1549 CD1 ILE 360
                              78.524 17.278 9.303 1.00 35.15
    ATOM 1550 C ILE 360
45
    ATOM 1551 O ILE 360
                              77.343 16.931 9.314 1.00 33.75
                               79.475 16.564 9.912 1.00 34.64
     ATOM 1552 N PRO 361
     ATOM 1553 CD PRO 361
                                80.930 16.785 9.873 1.00 35.59
     ATOM 1554 CA PRO 361
                                79.138 15.349 10.660 1.00 33.92
                               80.513 14.768 11.014 1.00 35.27
    ATOM 1555 CB PRO 361
                                81.412 15.972 11.048 1.00 35.97
50
    ATOM 1556 CG PRO 361
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ATOM 1557 C PRO 361
                               78.292 15.618 11.909 1.00 30.95
                               78.555 16.554 12.653 1.00 31.50
     ATOM 1558 O PRO 361
     ATOM 1559 N HIS 362
                              77.269 14.793 12.112 1.00 28.75
    ATOM 1560 CA HIS 362
                               76.378 14.900 13.263 1.00 30.25
    ATOM 1561 CB HIS 362
                               77.152 14.612 14.548 1.00 31.20
    ATOM 1562 CG HIS 362
                               78.075 13.441 14.440 1.00 33.72
                                77.826 12.122 14.275 1.00 34.55
    ATOM 1563 CD2 HIS 362
                                79.449 13.569 14.469 1.00 35.55
    ATOM 1564 ND1 HIS 362
                                80.006 12.377 14.322 1.00 35.28
    ATOM 1565 CE1 HIS 362
                                79.040 11.484 14.204 1.00 37.61
10
    ATOM 1566 NE2 HIS 362
    ATOM 1567 C HIS 362
                              75.742 16.275 13.368 1.00 29.44
     ATOM 1568 O HIS 362
                               75.521 16.769 14.472 1.00 29.93
     ATOM 1569 N PHE 363
                               75.397 16.856 12.222 1.00 29.22
    ATOM 1570 CA PHE 363
                               74.803 18.188 12.160 1.00 27.72
    ATOM 1571 CB PHE 363
                                74.446 18.538 10.709 1.00 26.85
15
                                73.901 19.931 10.532 1.00 27.48
    ATOM 1572 CG PHE 363
    ATOM 1573 CD1 PHE 363
                                74.758 21.017 10.391 1.00 27.76
                                72.523 20.157 10.513 1.00 27.45
     ATOM 1574 CD2 PHE 363
    ATOM 1575 CE1 PHE 363
                                74.244 22.313 10.234 1.00 28.56
20
    ATOM 1576 CE2 PHE 363
                                72.001 21.446 10.357 1.00 25.15
    ATOM 1577 CZ PHE 363
                               72.860 22.521 10.219 1.00 24.41
                               73.597 18.385 13.075 1.00 27.45
    ATOM 1578 C PHE 363
    ATOM 1579 O PHE 363
                               73.577 19.324 13.880 1.00 27.73
    ATOM 1580 N TRP 364
                               72.616 17.489 12.983 1.00 25.89
                               71.401 17.592 13.800 1.00 25.85
    ATOM 1581 CA TRP 364
25
    ATOM 1582 CB TRP 364
                                70.444 16.426 13.506 1.00 24.27
    ATOM 1583 CG TRP 364
                                69.168 16.391 14.328 1.00 23.75
    ATOM 1584 CD2 TRP 364
                                68.152 17.407 14.397 1.00 24.87
    ATOM 1585 CE2 TRP 364
                                67.140 16.922 15.261 1.00 24.81
30
    ATOM 1586 CE3 TRP 364
                                67.989 18.674 13.820 1.00 25.47
                                68.745 15.370 15.122 1.00 22.98
    ATOM 1587 CD1 TRP 364
    ATOM 1588 NE1 TRP 364
                                67.530 15.679 15.684 1.00 25.99
                                65.987 17.661 15.560 1.00 25.14
    ATOM 1589 CZ2 TRP 364
    ATOM 1590 CZ3 TRP 364
                                66.844 19.405 14.116 1.00 25.29
    ATOM 1591 CH2 TRP 364
                                65.857 18.894 14.982 1.00 24.53
35
    ATOM 1592 C TRP 364
                               71.659 17.747 15.308 1.00 26.94
    ATOM 1593 O TRP 364
                               71.202 18.721 15.904 1.00 27.16
    ATOM 1594 N PRO 365
                               72.382 16.796 15.944 1.00 27.60
    ATOM 1595 CD PRO 365
                                72.912 15.522 15.411 1.00 27.55
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    ATOM 1596 CA PRO 365
                                72.655 16.915 17.387 1.00 25.90
    ATOM 1597 CB PRO 365
                                73.565 15.717 17.668 1.00 26.00
    ATOM 1598 CG PRO 365
                                73.136 14.705 16.658 1.00 28.32
    ATOM 1599 C PRO 365
                               73.374 18.225 17.714 1.00 23.89
    ATOM 1600 O PRO 365
                               73.088 18.861 18.725 1.00 23.81
                               74.297 18.626 16.845 1.00 24.24
45
    ATOM 1601 N LYS 366
    ATOM 1602 CA LYS 366
                                75.058 19.862 17.027 1.00 26.24
    ATOM 1603 CB LYS 366
                                76.144 19.982 15.963 1.00 27.44
    ATOM 1604 CG LYS 366
                                77.310 19.022 16.138 1.00 28.76
    ATOM 1605 CD LYS 366
                                78.254 19.171 14.975 1.00 30.53
                               79.527 18.387 15.167 1.00 34.25
50
    ATOM 1606 CE LYS 366
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80.388 18.463 13.947 1.00 37.89
     ATOM 1607 NZ LYS 366
                               74.181 21.107 16.993 1.00 26.73
     ATOM 1608 C LYS 366
     ATOM 1609 O LYS 366
                               74.385 22.042 17.762 1.00 27.36
    ATOM 1610 N LEU 367
                               73.216 21.124 16.086 1.00 27.98
                               72.308 22.256 15.967 1.00 27.87
    ATOM 1611 CA LEU 367
 5
     ATOM 1612 CB LEU 367
                                71.559 22.192 14.632 1.00 27.29
                                70.613 23.356 14.318 1.00 27.25
     ATOM 1613 CG LEU 367
                                71.334 24.707 14.510 1.00 22.90
     ATOM 1614 CD1 LEU 367
                                70.081 23.189 12.896 1.00 24.54
     ATOM 1615 CD2 LEU 367
10
    ATOM 1616 C LEU 367
                               71.327 22.223 17.134 1.00 29.38
     ATOM 1617 O LEU 367
                               70.993 23.249 17.716 1.00 31.09
                               70.889 21.026 17.491 1.00 30.38
     ATOM 1618 N LEU 368
                                69.962 20.843 18.594 1.00 31.14
     ATOM 1619 CA LEU 368
     ATOM 1620 CB LEU 368
                                69.659 19.353 18.731 1.00 32.20
    ATOM 1621 CG LEU 368
                                68.247 18.852 19.014 1.00 33.52
15
                                67.184 19.651 18.267 1.00 31.14
     ATOM 1622 CD1 LEU 368
     ATOM 1623 CD2 LEU 368
                                68.210 17.379 18.632 1.00 33.99
                               70.601 21.395 19.876 1.00 32.36
     ATOM 1624 C LEU 368
                               69.917 21.963 20.730 1.00 32.58
     ATOM 1625 O LEU 368
20
     ATOM 1626 N MET 369
                               71.922 21.272 19.985 1.00 33.30
                                72.641 21.771 21.149 1.00 34.04
     ATOM 1627 CA MET 369
     ATOM 1628 CB MET 369
                                74.051 21.190 21.209 1.00 35.31
     ATOM 1629 CG MET 369
                                74.108 19.858 21.935 1.00 36.83
     ATOM 1630 SD MET 369
                                75.312 18.728 21.235 1.00 43.07
                                76.862 19.636 21.472 1.00 41.31
25
     ATOM 1631 CE MET 369
     ATOM 1632 C MET 369
                               72.675 23.297 21.212 1.00 34.30
     ATOM 1633 O MET 369
                               72.961 23.876 22.269 1.00 35.82
                               72.368 23.949 20.091 1.00 32.14
     ATOM 1634 N LYS 370
     ATOM 1635 CA LYS 370
                                72.325 25.405 20.044 1.00 29.17
30
    ATOM 1636 CB LYS 370
                                72.394 25.904 18.608 1.00 28.18
                                73.662 25.518 17.900 1.00 27.72
     ATOM 1637 CG LYS 370
                                74.866 25.969 18.679 1.00 28.10
     ATOM 1638 CD LYS 370
                               76.127 25.650 17.930 1.00 27.79
     ATOM 1639 CE LYS 370
    ATOM 1640 NZ LYS 370
                                77.298 25.941 18.777 1.00 30.78
                               71.033 25.875 20.705 1.00 29.27
     ATOM 1641 C LYS 370
35
     ATOM 1642 O LYS 370
                               70.950 26.999 21.200 1.00 29.43
                               70.018 25.014 20.714 1.00 29.40
     ATOM 1643 N VAL 371
     ATOM 1644 CA VAL 371
                                68.756 25.358 21.358 1.00 29.90
                                67.687 24.237 21.218 1.00 28.75
     ATOM 1645 CB VAL 371
40
     ATOM 1646 CG1 VAL 371
                                66,463 24,561 22,064 1,00 27,12
                                67.275 24.080 19.762 1.00 29.23
     ATOM 1647 CG2 VAL 371
     ATOM 1648 C VAL 371
                               69.075 25.573 22.832 1.00 31.39
     ATOM 1649 O VAL 371
                               68.543 26.481 23.462 1.00 31.20
     ATOM 1650 N THR 372
                               69.971 24.743 23.366 1.00 31.39
                               70.371 24.847 24.762 1.00 31.10
45
    ATOM 1651 CA THR 372
                                71.282 23.664 25.170 1.00 31.59
     ATOM 1652 CB THR 372
     ATOM 1653 OG1 THR 372
                                70,554 22,441 25,008 1,00 30,60
                               71.720 23.795 26.625 1.00 30.14
     ATOM 1654 CG2 THR 372
                               71.071 26.186 24.994 1.00 30.76
     ATOM 1655 C THR 372
                               70.711 26.935 25.910 1.00 31.45
    ATOM 1656 O THR 372
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72.038 26.507 24.138 1.00 29.31
    ATOM 1657 N ASP 373
                               72.744 27.772 24.252 1.00 27.32
    ATOM 1658 CA ASP 373
                               73.745 27.934 23.115 1.00 27.98
    ATOM 1659 CB ASP 373
                               74.886 26.933 23.190 1.00 28.94
    ATOM 1660 CG ASP 373
                                75.043 26.259 24.225 1.00 31.01
    ATOM 1661 OD1 ASP 373
    ATOM 1662 OD2 ASP 373
                                75.639 26.825 22.205 1.00 31.38
                              71.742 28.926 24.247 1.00 26.50
    ATOM 1663 C ASP 373
                               71.872 29.861 25.040 1.00 27.35
    ATOM 1664 O ASP 373
    ATOM 1665 N LEU 374
                               70.711 28.826 23.412 1.00 24.17
    ATOM 1666 CA LEU 374
                               69.688 29.864 23.331 1.00 23.38
10
                               68.795 29.660 22.107 1.00 22.98
    ATOM 1667 CB LEU 374
    ATOM 1668 CG LEU 374
                                69.361 30.183 20.786 1.00 24.45
    ATOM 1669 CD1 LEU 374
                                68.668 29.520 19.589 1.00 24.72
                                69.223 31.704 20.735 1.00 22.40
    ATOM 1670 CD2 LEU 374
                               68.839 29.964 24.589 1.00 24.31
    ATOM 1671 C LEU 374
15
                               68.442 31.065 24.986 1.00 23.31
    ATOM 1672 O LEU 374
    ATOM 1673 N ARG 375
                               68.543 28.826 25.211 1.00 25.32
                                67.748 28.821 26.438 1.00 27.76
    ATOM 1674 CA ARG 375
                                67.455 27.392 26.908 1.00 30.82
    ATOM 1675 CB ARG 375
                                66.901 26.439 25.854 1.00 38.79
20
    ATOM 1676 CG ARG 375
                                65.424 26.630 25.582 1.00 45.40
    ATOM 1677 CD ARG 375
    ATOM 1678 NE ARG 375
                                64.709 25.360 25.620 1.00 52.61
                                63.800 24.967 24.726 1.00 56.89
    ATOM 1679 CZ ARG 375
                                63.473 25.732 23.694 1.00 58.27
    ATOM 1680 NH1 ARG 375
    ATOM 1681 NH2 ARG 375
                                 63.201 23.793 24.855 1.00 58.46
25
                               68.563 29.542 27.512 1.00 26.98
    ATOM 1682 C ARG 375
                               68.025 30.336 28.282 1.00 26.18
    ATOM 1683 O ARG 375
     ATOM 1684 N MET 376
                               69.862 29.255 27.551 1.00 26.80
    ATOM 1685 CA MET 376
                                70.767 29.867 28.511 1.00 29.22
                                72.172 29.270 28.379 1.00 33.70
    ATOM 1686 CB MET 376
30
     ATOM 1687 CG MET 376
                                72.595 28.371 29.562 1.00 43.20
    ATOM 1688 SD MET 376
                                73.320 29.260 31.011 1.00 52.38
     ATOM 1689 CE MET 376
                                71.843 29.854 31.913 1.00 48.11
                               70.804 31.384 28.339 1.00 27.54
    ATOM 1690 C MET 376
    ATOM 1691 O MET 376
                               70.792 32.126 29.323 1.00 26.96
35
                              70.841 31.835 27.087 1.00 25.39
    ATOM 1692 N ILE 377
     ATOM 1693 CA ILE 377
                               70.847 33.264 26.767 1.00 23.26
                               70.992 33.488 25.222 1.00 22.73
     ATOM 1694 CB ILE 377
                               70.560 34.909 24.819 1.00 21.81
     ATOM 1695 CG2 ILE 377
                               72.431 33.205 24.789 1.00 20.39
40
     ATOM 1696 CG1 ILE 377
                                72.644 33.148 23.300 1.00 18.85
     ATOM 1697 CD1 ILE 377
     ATOM 1698 C ILE 377
                              69.558 33.900 27.309 1.00 22.91
                              69.597 34.925 27.989 1.00 22.02
     ATOM 1699 O ILE 377
     ATOM 1700 N GLY 378
                               68.427 33.244 27.069 1.00 22.29
                                67.161 33.757 27.547 1.00 22.83
     ATOM 1701 CA GLY 378
45
     ATOM 1702 C GLY 378
                               67.111 33.815 29.063 1.00 25.60
     ATOM 1703 O GLY 378
                               66.546 34.752 29.630 1.00 26.25
     ATOM 1704 N ALA 379
                               67.691 32.804 29.713 1.00 26.88
                              67.744 32.707 31.175 1.00 27.19
     ATOM 1705 CA ALA 379
                                68.322 31.358 31.590 1.00 26.97
50
    ATOM 1706 CB ALA 379
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ATOM 1707 C ALA 379
                               68.606 33.827 31.738 1.00 26.13
                               68.174 34.580 32.601 1.00 26.46
    ATOM 1708 O ALA 379
                               69.826 33.935 31.230 1.00 27.61
    ATOM 1709 N CYA 380
    ATOM 1710 CA CYA 380
                                70.742 34.973 31.667 1.00 29.74
                                72.070 34.865 30.923 1.00 35.44
    ATOM 1711 CB CYA 380
                                73.081 33.458 31.417 1.00 42.61
    ATOM 1712 SG CYA 380
                                74.829 33.691 29.945 1.00 55.91
    ATOM 1713 AS CYA 380
                               70.142 36.349 31.446 1.00 29.07
    ATOM 1714 C CYA 380
    ATOM 1715 O CYA 380
                               70.243 37.225 32.303 1.00 29.46
                              69.494 36.538 30.304 1.00 28.29
    ATOM 1716 N HIS 381
10
                               68.885 37.824 30.002 1.00 26.84
    ATOM 1717 CA HIS 381
                               68.384 37.880 28.557 1.00 23.13
    ATOM 1718 CB HIS 381
                               67.597 39.113 28.259 1.00 19.84
    ATOM 1719 CG HIS 381
                               67.993 40.365 27.931 1.00 18.68
    ATOM 1720 CD2 HIS 381
    ATOM 1721 ND1 HIS 381
                                66.229 39.169 28.403 1.00 19.47
15
                               65.817 40.407 28.190 1.00 18.64
    ATOM 1722 CE1 HIS 381
                                66.868 41.149 27.900 1.00 18.29
    ATOM 1723 NE2 HIS 381
    ATOM 1724 C HIS 381
                              67.747 38.157 30.967 1.00 26.78
                              67.560 39.314 31.337 1.00 26.39
    ATOM 1725 O HIS 381
                               66.964 37.158 31.347 1.00 27.78
     ATOM 1726 N ALA 382
20
                                65.867 37.395 32.269 1.00 29.45
    ATOM 1727 CA ALA 382
     ATOM 1728 CB ALA 382
                                65.077 36.125 32.471 1.00 29.51
                               66.425 37.904 33.604 1.00 31.74
     ATOM 1729 C ALA 382
     ATOM 1730 O ALA 382
                               65.932 38.882 34.159 1.00 32.60
                               67.483 37.262 34.093 1.00 33.02
     ATOM 1731 N SER 383
25
                                68.109 37.662 35.350 1.00 34.69
     ATOM 1732 CA SER 383
     ATOM 1733 CB SER 383
                                69.212 36.677 35.733 1.00 36.18
                                68.663 35.386 35.933 1.00 40.61
     ATOM 1734 OG SER 383
                               68.689 39.064 35.242 1.00 33.49
     ATOM 1735 C SER 383
                               68.526 39.889 36.146 1.00 34.28
     ATOM 1736 O SER 383
30
                               69.377 39.332 34.141 1.00 32.60
     ATOM 1737 N ARG 384
                                69.955 40.642 33.938 1.00 32.60
     ATOM 1738 CA ARG 384
                                70.926 40.638 32.762 1.00 33.60
     ATOM 1739 CB ARG 384
                                71.429 42.013 32.409 1.00 36.33
     ATOM 1740 CG ARG 384
                                72.875 41.975 31.993 1.00 39.62
     ATOM 1741 CD ARG 384
35
     ATOM 1742 NE ARG 384
                                73.760 42.260 33.114 1.00 41.76
                                74.587 43.301 33.179 1.00 41.92
     ATOM 1743 CZ ARG 384
                                 74.670 44.182 32.191 1.00 40.66
     ATOM 1744 NH1 ARG 384
     ATOM 1745 NH2 ARG 384
                                 75.319 43.471 34.260 1.00 44.88
     ATOM 1746 C ARG 384
                               68.862 41.694 33.758 1.00 32.28
40
     ATOM 1747 O ARG 384
                                69.014 42.831 34.213 1.00 33.27
                               67.739 41.311 33.159 1.00 29.13
     ATOM 1748 N PHE 385
                                66.663 42.259 32.977 1.00 27.55
     ATOM 1749 CA PHE 385
     ATOM 1750 CB PHE 385
                                65.552 41.687 32.105 1.00 26.89
                                64.415 42.641 31.888 1.00 25.11
     ATOM 1751 CG PHE 385
45
                                64.495 43.630 30.918 1.00 24.94
     ATOM 1752 CD1 PHE 385
                                63.281 42.580 32.689 1.00 25.01
     ATOM 1753 CD2 PHE 385
                                63.466 44.547 30.753 1.00 25.50
     ATOM 1754 CE1 PHE 385
                                62.244 43.495 32.531 1.00 24.06
     ATOM 1755 CE2 PHE 385
     ATOM 1756 CZ PHE 385
                                62.338 44.482 31.563 1.00 25.44
50
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66.125 42.641 34.348 1.00 29.08
    ATOM 1757 C PHE 385
    ATOM 1758 O PHE 385
                              65.887 43.816 34.613 1.00 27.90
                               65.972 41.658 35.231 1.00 31.19
    ATOM 1759 N LEU 386
                               65.465 41.929 36.577 1.00 33.22
    ATOM 1760 CA LEU 386
    ATOM 1761 CB LEU 386
                               65.355 40.640 37.397 1.00 34.35
    ATOM 1762 C LEU 386
                              66.362 42.940 37.279 1.00 33.52
                               65.874 43.907 37.855 1.00 32.93
    ATOM 1763 O LEU 386
                              67.673 42.760 37.158 1.00 34.80
    ATOM 1764 N HIS 387
    ATOM 1765 CA HIS 387
                               68.628 43.674 37.775 1.00 37.88
                               70.042 43.112 37.705 1.00 36.66
    ATOM 1766 CB HIS 387
10
                               70.206 41.832 38.456 1.00 39.14
    ATOM 1767 CG HIS 387
                               69.307 41.080 39.144 1.00 39.28
    ATOM 1768 CD2 HIS 387
    ATOM 1769 ND1 HIS 387
                               71.408 41.161 38.543 1.00 40.97
                               71.241 40.055 39.245 1.00 41.57
    ATOM 1770 CE1 HIS 387
                               69.980 39.984 39.618 1.00 41.45
    ATOM 1771 NE2 HIS 387
15
                              68.589 45.071 37.164 1.00 40.38
    ATOM 1772 C HIS 387
                              68.673 46.054 37.888 1.00 40.87
    ATOM 1773 O HIS 387
                               68.466 45.161 35.842 1.00 43.32
    ATOM 1774 N MET 388
                                68.398 46.455 35.168 1.00 46.28
    ATOM 1775 CA MET 388
                                68.170 46.286 33.665 1.00 43.30
    ATOM 1776 CB MET 388
20
    ATOM 1777 CG MET 388
                                69.342 45.738 32.875 1.00 43.55
                                69.034 45.896 31.098 1.00 46.27
    ATOM 1778 SD MET 388
                               68.208 44.370 30.709 1.00 42.36
    ATOM 1779 CE MET 388
                               67.256 47.289 35.737 1.00 50.25
    ATOM 1780 C MET 388
                               67.363 48.506 35.886 1.00 49.79
25
    ATOM 1781 O MET 388
                               66.163 46.610 36.075 1.00 52.74
    ATOM 1782 N LYS 389
                                                             ALTA
                               64.983 47.274 36.633 1.00 56.15
                                                              ALTA
    ATOM 1783 CA LYS 389
                               63.770 46.334 36.565 1.00 56.87
                                                              ALTA
    ATOM 1784 CB LYS 389
    ATOM 1785 CG LYS 389
                               63.227 46.087 35.161 1.00 57.76
                                                              ALTA
                               62.029 45.156 35.212 1.00 55.98
                                                              ALTA
    ATOM 1786 CD LYS 389
30
                               62.426 43.796 35.778 1.00 55.48
                                                              ALTA
     ATOM 1787 CE LYS 389
                               61.267 43.040 36.311 1.00 55.55
                                                              ALTA
    ATOM 1788 NZ LYS 389
    ATOM 1789 C LYS 389
                               65.177 47.767 38.064 1.00 56.69
                                                             ALTA
    ATOM 1790 O LYS 389
                               64.623 48.814 38.453 1.00 58.54
                                                             ALTA
                               65.955 47.038 38.839 1.00 55.21
    ATOM 1791 N VAL 390
35
     ATOM 1792 CA VAL 390
                                66,225 47,386 40,236 1,00 51,78
    ATOM 1793 CB VAL 390
                                66.999 46.231 40.985 1.00 50.07
                               67.648 46.726 42.263 1.00 49.74
     ATOM 1794 CG1 VAL 390
                                66.037 45.093 41.317 1.00 49.06
     ATOM 1795 CG2 VAL 390
     ATOM 1796 C VAL 390
                               67.053 48.681 40.227 1.00 49.38
40
                               66.785 49.605 40.992 1.00 48.71
     ATOM 1797 O VAL 390
     ATOM 1798 N GLU 391
                               67.974 48.778 39.272 1.00 46.71
                                68.866 49.919 39.142 1.00 44.88
     ATOM 1799 CA GLU 391
     ATOM 1800 CB GLU 391
                                70.156 49.488 38.438 1.00 45.24
     ATOM 1801 CG GLU 391
                                70.793 48.207 38.997 1.00 47.65
45
                                71.461 48.388 40.358 1.00 50.29
     ATOM 1802 CD GLU 391
                               71.141 49.373 41.063 1.00 50.68
     ATOM 1803 OE1 GLU 391
     ATOM 1804 OE2 GLU 391
                                72.310 47.535 40.718 1.00 50.85
                               68.324 51.174 38.458 1.00 45.28
     ATOM 1805 C GLU 391
                               68.568 52.286 38.940 1.00 46.46
50
     ATOM 1806 O GLU 391
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67.568 51.024 37.372 1.00 43.33
    ATOM 1807 N CYA 392
    ATOM 1808 CA CYA 392
                               67.071 52.192 36.643 1.00 42.28
                               67.519 52.096 35.197 1.00 42.45
    ATOM 1809 CB CYA 392
                               69.280 52.182 35.127 1.00 43.69
    ATOM 1810 SG CYA 392
                               69.908 51.044 33.336 1.00 48.17
    ATOM 1811 AS CYA 392
5
                               65.589 52.493 36.709 1.00 42.51
    ATOM 1812 C CYA 392
                               64.792 51.634 37.070 1.00 43.30
    ATOM 1813 O CYA 392
    ATOM 1814 N PRO 393
                               65.205 53.752 36.418 1.00 42.13
    ATOM 1815 CD PRO 393
                               66.109 54.899 36.199 1.00 40.54
    ATOM 1816 CA PRO 393
                               63.794 54.182 36.441 1.00 42.26
10
    ATOM 1817 CB PRO 393
                               63.896 55.710 36.365 1.00 41.47
                               65.189 55.938 35.614 1.00 41.10
    ATOM 1818 CG PRO 393
                              62.954 53.606 35.281 1.00 43.20
    ATOM 1819 C PRO 393
    ATOM 1820 O PRO 393
                               63.463 53.452 34.163 1.00 42.61
                               61.686 53.305 35.559 1.00 43.70
    ATOM 1821 N THR 394
15
    ATOM 1822 CA THR 394
                               60.764 52.755 34.564 1.00 45.50
    ATOM 1823 CB THR 394
                               59.340 52.609 35.129 1.00 47.20
                               59.304 53.139 36.464 1.00 50.57
     ATOM 1824 OG1 THR 394
    ATOM 1825 CG2 THR 394
                               58.878 51.150 35.137 1.00 47.99
                               60.682 53.583 33.283 1.00 44.58
    ATOM 1826 C THR 394
20
                               60.409 53.054 32.215 1.00 46.36
    ATOM 1827 O THR 394
                               60.899 54.888 33.396 1.00 42.88
    ATOM 1828 N GLU 395
                                60.842 55.790 32.246 1.00 40.54
    ATOM 1829 CA GLU 395
                               61.096 57.234 32.699 1.00 40.69
    ATOM 1830 CB GLU 395
                               61.799 55.421 31.098 1.00 38.51
25
    ATOM 1831 C GLU 395
    ATOM 1832 O GLU 395
                               61.628 55.877 29.968 1.00 39.41
                               62.828 54.640 31.402 1.00 35.60
     ATOM 1833 N LEU 396
                               63.795 54.220 30.386 1.00 33.11
     ATOM 1834 CA LEU 396
    ATOM 1835 CB LEU 396
                               65.169 54.003 31.027 1.00 33.60
                                65.831 55.230 31.660 1.00 34.54
    ATOM 1836 CG LEU 396
30
     ATOM 1837 CD1 LEU 396
                               67.160 54.835 32.282 1.00 32.83
                                66.026 56.308 30.599 1.00 35.71
     ATOM 1838 CD2 LEU 396
                               63.388 52.940 29.660 1.00 30.95
     ATOM 1839 C LEU 396
     ATOM 1840 O LEU 396
                               63.950 52.605 28.624 1.00 30.90
                               62.422 52.227 30.223 1.00 30.18
    ATOM 1841 N PHE 397
35
                               61.961 50.970 29.654 1.00 28.80
     ATOM 1842 CA PHE 397
                               61.712 49.946 30.777 1.00 28.10
     ATOM 1843 CB PHE 397
                               62.938 49.604 31.592 1.00 28.96
     ATOM 1844 CG PHE 397
     ATOM 1845 CD1 PHE 397
                                63.403 50.472 32.591 1.00 28.39
                                63.636 48.422 31.359 1.00 26.28
     ATOM 1846 CD2 PHE 397
40
     ATOM 1847 CE1 PHE 397
                                64.546 50.166 33.337 1.00 28.44
     ATOM 1848 CE2 PHE 397
                                64.784 48.107 32.103 1.00 29.21
                               65.240 48.984 33.096 1.00 27.37
     ATOM 1849 CZ PHE 397
                               60.683 51.093 28.836 1.00 27.54
     ATOM 1850 C PHE 397
     ATOM 1851 O PHE 397
                               59.630 51.431 29.370 1.00 26.96
45
                               60.753 50.836 27.501 1.00 27.41
     ATOM 1852 N PRO 398
                               61.968 50.600 26.686 1.00 25.42
     ATOM 1853 CD PRO 398
                                59.560 50.920 26.654 1.00 25.90
     ATOM 1854 CA PRO 398
                               60.068 50.383 25.320 1.00 25.26
     ATOM 1855 CB PRO 398
                                61.490 50.893 25.290 1.00 23.99
    ATOM 1856 CG PRO 398
50
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ATOM 1857 C PRO 398
                               58.494 49.995 27.272 1.00 25.86
                               58.839 48.962 27.843 1.00 25.82
    ATOM 1858 O PRO 398
                               57.197 50.355 27.175 1.00 25.52
    ATOM 1859 N PRO 399
                              56.627 51.576 26.578 1.00 25.49
    ATOM 1860 CD PRO 399
                               56.145 49.510 27.754 1.00 25.42
    ATOM 1861 CA PRO 399
 5
    ATOM 1862 CB PRO 399
                               54.861 50.181 27.273 1.00 26.23
                               55.237 51.609 27.156 1.00 25.25
    ATOM 1863 CG PRO 399
    ATOM 1864 C PRO 399
                               56.198 48.043 27.317 1.00 26.08
    ATOM 1865 O PRO 399
                               56.132 47.131 28.159 1.00 25.45
                               56.350 47.810 26.019 1.00 25.57
    ATOM 1866 N LEU 400
10
                               56.406 46.440 25.509 1.00 26.27
    ATOM 1867 CA LEU 400
                               56.404 46.418 23.980 1.00 25.03
    ATOM 1868 CB LEU 400
    ATOM 1869 CG LEU 400
                               56.117 45.042 23.363 1.00 24.51
                                54.757 44.530 23.806 1.00 23.22
    ATOM 1870 CD1 LEU 400
    ATOM 1871 CD2 LEU 400
                                56.173 45.149 21.862 1.00 23.70
15
    ATOM 1872 C LEU 400
                               57.602 45.657 26.067 1.00 27.06
                               57.484 44.465 26.363 1.00 27.41
    ATOM 1873 O LEU 400
                               58.736 46.339 26.231 1.00 27.16
    ATOM 1874 N PHE 401
    ATOM 1875 CA PHE 401
                              59.966 45.754 26.779 1.00 27.06
                               61.047 46.833 26.802 1.00 26.60
20
    ATOM 1876 CB PHE 401
                               62.408 46.351 27.217 1.00 28.08
    ATOM 1877 CG PHE 401
     ATOM 1878 CD1 PHE 401
                               62.918 45.138 26.747 1.00 27.45
                                63.223 47.165 28.013 1.00 27.48
    ATOM 1879 CD2 PHE 401
                                64.220 44.746 27.055 1.00 26.95
    ATOM 1880 CE1 PHE 401
    ATOM 1881 CE2 PHE 401
                                64.523 46.786 28.327 1.00 27.97
25
                               65.028 45.575 27.846 1.00 28.46
    ATOM 1882 CZ PHE 401
    ATOM 1883 C PHE 401
                               59.690 45.247 28.205 1.00 27.62
                               60.046 44.125 28.570 1.00 26.24
     ATOM 1884 O PHE 401
     ATOM 1885 N LEU 402
                               59.036 46.082 29.002 1.00 28.75
                              58.692 45.719 30.366 1.00 29.58
    ATOM 1886 CA LEU 402
30
                               58.064 46.910 31.088 1.00 30.04
    ATOM 1887 CB LEU 402
                                59.025 47.974 31.594 1.00 30.14
    ATOM 1888 CG LEU 402
     ATOM 1889 CD1 LEU 402
                                58.270 49.263 31.880 1.00 29.61
                                59.734 47.438 32.827 1.00 27.99
     ATOM 1890 CD2 LEU 402
     ATOM 1891 C LEU 402
                               57.693 44.583 30.368 1.00 30.10
35
                               57.836 43.631 31.121 1.00 29.78
     ATOM 1892 O LEU 402
     ATOM 1893 N GLU 403
                               56.688 44.683 29.510 1.00 30.49
                              55.646 43.671 29.453 1.00 32.60
     ATOM 1894 CA GLU 403
                                54.562 44.094 28.469 1.00 37.01
     ATOM 1895 CB GLU 403
                                53.329 43.218 28.520 1.00 44.01
40
     ATOM 1896 CG GLU 403
                                52.263 43.632 27.523 1.00 48.50
     ATOM 1897 CD GLU 403
                               52.516 44.525 26.677 1.00 49.66
     ATOM 1898 OE1 GLU 403
                                51.157 43.050 27.594 1.00 53.06
     ATOM 1899 OE2 GLU 403
                               56.083 42.237 29.151 1.00 32.03
     ATOM 1900 C GLU 403
     ATOM 1901 O GLU 403
                               55.627 41.304 29.816 1.00 32.58
45
                               56.955 42.078 28.159 0.50 31.51
                                                             ALTA
     ATOM 1902 N VAL 404
     ATOM 1903 CA VAL 404
                              57,450 40.765 27.739 0.50 30.96
                                                              ALTA
     ATOM 1904 CB VAL 404
                                58.108 40.849 26.333 0.50 30.32
                                                              ALTA
     ATOM 1905 CG1 VAL 404 58.616 39.489 25.889 0.50 28.72
                                                              ALTA
                               57.115 41.388 25.328 0.50 31.67
     ATOM 1906 CG2 VAL 404
                                                              ALTA
50
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58.465 40.149 28.696 0.50 30.45
                                                               ALTA
     ATOM 1907 C VAL 404
     ATOM 1908 O VAL 404
                                58.549 38.926 28.822 0.50 30.10
                                                               ALTA
                               59.224 41.002 29.369 1.00 30.16
     ATOM 1909 N PHE 405
                                60.266 40.549 30.263 1.00 30.65
     ATOM 1910 CA PHE 405
     ATOM 1911 CB PHE 405
                                61.577 41.221 29.863 1.00 28.92
                                62.062 40.834 28.493 1.00 26.31
     ATOM 1912 CG PHE 405
                                62.342 41.804 27.543 1.00 25.72
     ATOM 1913 CD1 PHE 405
    ATOM 1914 CD2 PHE 405
                                 62.269 39.500 28.166 1.00 25.92
                                62.827 41.456 26.278 1.00 26.78
     ATOM 1915 CE1 PHE 405
                                62.752 39.139 26.910 1.00 25.39
     ATOM 1916 CE2 PHE 405
10
                                63.034 40.122 25.962 1.00 24.39
     ATOM 1917 CZ PHE 405
                               60.011 40.674 31.771 1.00 32.10
     ATOM 1918 C PHE 405
                               60,903 40,237 32,533 1.00 33.88
     ATOM 1919 O PHE 405
                                 58.936 41.169 32.188 1.00 34.95
     ATOM
           1920 OXT PHE 405
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             6 O1 HOH 506
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             54 O1 HOH 554
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             56 O1 HOH 556
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             64 O1 HOH 564
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             68 O1 HOH 568
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             69 O1 HOH 569
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             74 O1 HOH 574
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             76 O1 HOH 576
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             86 O1 HOH 586
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             90 O1 HOH 590
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             94 O1 HOH 594
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     ATOM 108 O1 HOH 608
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     ATOM 113 O1 HOH 613
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     ATOM 2039 O ACY 701
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     ATOM 2040 OXT ACY 701
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     ATOM 2041 CH3 ACY 701
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                              66.961 42.243 18.491 1.00 22.34
     ATOM 2050 C1 T3
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                              68.748 43.593 23.015 1.00 21.84
     ATOM 2051 C2 T3
                          1
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     ATOM 2052 C3 T3
                          1
                              69.252 44.540 23.871 1.00 22.31
     ATOM 2053 C4 T3
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     ATOM 2054 C5 T3
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     ATOM 2055 C6 T3
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     ATOM 2056 C7 T3
                              68.541 43.108 20.632 1.00 24.65
                          1
                              67.895 43.567 25.639 1.00 21.93
     ATOM 2057 C8 T3
                          1
                              68.665 41.792 20.183 1.00 25.09
     ATOM 2058 C9 T3
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     ATOM 2059 C10 T3
                              67.427 42.654 24.733 1.00 23.66
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                          1
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     ATOM 2060 C11 T3
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                              67.829 42.624 23.384 1.00 19.67
     ATOM 2061 C12 T3
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                              66.055 41.788 17.371 1.00 18.97
     ATOM 2062 C13 T3
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     ATOM 2063 C15 T3
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    ATOM 2066 I2 T3
                            70.019 40.450 20.975 1.00 25.67
    ATOM 2067 I3 T3
    ATOM 2068 N1 T3
                             68.131 41.337 16.037 1.00 15.12
                             67.542 43.587 26.966 1.00 21.79
    ATOM 2069 O1 T3
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                        1
                             69.259 43.600 21.682 1.00 22.05
    ATOM 2070 O2 T3
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                             66.504 40.852 13.963 1.00 20.38
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                             64.675 40.731 15.192 1.00 20.16
    ATOM 2072 O4 T3
    END
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10

## **APPENDIX 7**

## TRBTRIAC.PDB

REMARK TR-beta Triac Full length numbering

REMARK refinement resolution: 100 - 2.9 A r= 0.273258 free\_r= 0.333794

5 REMARK wa= 5.78307

REMARK target= mlf cycles= 1 steps= 25

REMARK a= 68.72 b= 68.72 c= 130.092 alpha= 90 beta= 90 gamma= 120

REMARK ncs= none

REMARK initial B-factor correction: "none"

10 REMARK ALA 199 to ALA 201 from His-tag

REMARK

REMARK Four cacodylate-modified cysteines (CYA)

REMARK Cys294, Cys298, Cys388, Cys434

REMARK cacodylate modeled as single arsenic atom

15 REMARK

REMARK side chain of certain residues modeled as ALA due to poor density;

REMARK however, residue name reflects true residue for clarity

**REMARK** 

REMARK amino acid sequence confirmed,

20 REMARK differing from that reported by Weinberger et. al.

REMARK in the following codons:

REMARK 243 Pro - Arg

REMARK 337 lle - Thr

REMARK 451 Leu - Phe

25 REMARK as reported by Sakurai et. al.

REMARK note also correction of initiation codon,

REMARK yielding a polypeptide of 461 amino acids

JRNL AUTH A.SAKURAI, A.NAKAI, L.J. DEGROOT

JRNL TITL STRUCTURAL ANALYSIS OF HUMAN THYROID HORMONE

30 RECEPTOR

JRNL TITL2 BETA GENE

JRNL REF MOL.CELL.ENDO. V.71 1990

JRNL AUTH

C.WEINBERGER,

C.C.THOMPSON,R.LEBO,D.J.GRUOL,R.M.EVANS

35 JRNL TITL THE C-ERB-A GENE ENCODES A THYROID HORMONE RECEPTOR

JRNL REF NATURE

V.324 6098 1986

	ATOM	1 CB ALA 199	31.247 28.289 43.613 1.00 71.30	PROT
40	ATOM	2 C ALA 199	32.916 26.485 44.170 1.00 68.99	PROT
	ATOM	3 O ALA 199	33.485 25.410 43.976 1.00 63.84	PROT
	ATOM	4 N ALA 199	30.462 25.993 44.096 1.00 75.00	PROT
	ATOM	5 CA ALA 199	31.571 26.795 43.497 1.00 73.24	PROT
45	ATOM	6 N ALA 200	33.419 27.432 44.958 1.00 73.81	PROT
	ATOM	7 CA ALA 200	34.686 27.251 45.658 1.00 67.87	PROT
	ATOM	8 CB ALA 200	35.182 28.583 46.203 1.00 62.83	PROT
	ATOM	9 C ALA 200	34.539 26.239 46.791 1.00 63.23	PROT
	ATOM	10 O ALA 200	35.486 25.986 47.534 1.00 59.14	PROT

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PROT
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             12 CA ALA 201
                                                              PROT
             13 CB ALA 201
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             14 C ALA 201
                              34.248 23.662 47.762 1.00 53.15
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     ATOM
             15 O ALA 201
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             16 N GLU 202
             17 CA GLU 202
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             18 CB GLU 202
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             19 CG GLU 202
     ATOM
             20 CD GLU 202
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     ATOM
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             21 OE1 GLU 202
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             22 OE2 GLU 202
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             24 O GLU 202
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     ATOM
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                               38.603 26.683 47.079 1.00 28.28
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             30 N LEU 204
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             31 CA LEU 204
             32 CB LEU 204
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             33 CG LEU 204
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                                                              PROT
     ATOM
                                                              PROT
             34 CD1 LEU 204
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                                                              PROT
             35 CD2 LEU 204
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             36 C LEU 204
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     ATOM
             40 CB GLN 205
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             46 O GLN 205
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             51 O LYS 206
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             52 N SER 207
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             53 CA SER 207
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             54 CB SER 207
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             57 O SER 207
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             59 CA ILE 208
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     ATOM
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             62 CG1 ILE 208
                                                              PROT
     ATOM
             63 CD1 ILE 208
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             67 CA GLY 209
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             69 O GLY 209
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             71 CA HIS 210
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             72 CB HIS 210
                                                             PROT
     ATOM
                              38.959 15.806 50.266 1.00 27.75
                                                            PROT
     ATOM
             73 C HIS 210
     ATOM
             74 O HIS 210
                              39.328 16.741 49.550 1.00 34.08
                                                            PROT
             75 N LYS 211
                              38.807 14.566 49.805 1.00 16.50
                                                             PROT
15
     ATOM
                               39.019 14.206 48.403 1.00 5.57
             76 CA LYS 211
                                                             PROT
     ATOM
     ATOM
             77 CB LYS 211
                               39.932 12.981 48.295 1.00 5.67
                                                             PROT
             78 CG LYS 211
                               41.370 13.208 48.742 1.00 7.30
     ATOM
                                                             PROT
             79 CD LYS 211
                               41.873 14.594 48.347 1.00 14.34
                                                              PROT
     ATOM
                               43.339 14.556 47.897 1.00 29.48
20
     ATOM
             80 CE LYS 211
                                                              PROT
             81 NZ LYS 211
                               43.777 15.851 47.262 1.00 33.43
     ATOM
                                                             PROT
             82 C LYS 211
                              37.642 13.861 47.876 1.00 2.73
     ATOM
                                                            PROT
                              37.176 12.741 48.039 1.00 6.57
                                                             PROT
             83 O LYS 211
     ATOM
     ATOM
             84 N PRO 212
                              36.983 14.813 47.208 1.00 2.00
                                                             PROT
                               37.472 16.156 46.846 1.00 10.43
                                                              PROT
             85 CD PRO 212
25
     ATOM
                               35.642 14.542 46.689 1.00 2.05
             86 CA PRO 212
                                                             PROT
     ATOM
                               35.088 15.928 46.341 1.00 10.09
     ATOM
             87 CB PRO 212
                                                              PROT
                               36.240 16.888 46.422 1.00 8.43
             88 CG PRO 212
                                                             PROT
     ATOM
             89 C PRO 212
                              35.523 13.578 45.520 1.00 2.00
                                                             PROT
     ATOM
30
     ATOM
             90 O PRO 212
                              36.344 13.554 44.611 1.00 6.04
                                                             PROT
             91 N GLU 213
                              34.476 12.773 45.577 1.00 2.68
                                                             PROT
     ATOM
             92 CA GLU 213
                               34.181 11.817 44.542 1.00 6.81
                                                             PROT
     ATOM
             93 CB GLU 213
                               33.539 10.594 45.173 1.00 7.20
                                                             PROT
     ATOM
                               34.222 10.232 46.462 1.00 15.33
                                                              PROT
     ATOM
             94 CG GLU 213
             95 CD GLU 213
                               34.293 8.743 46.689 1.00 21.36
                                                              PROT
35
     ATOM
                                33.334 8.051 46.290 1.00 29.32
                                                              PROT
     ATOM
             96 OE1 GLU 213
     ATOM
             97 OE2 GLU 213
                                35.301 8.265 47.268 1.00 28.50
                                                              PROT
             98 C GLU 213
                              33.229 12.543 43.584 1.00 12.00
     ATOM
                                                             PROT
             99 O GLU 213
                              32.693 13.599 43.926 1.00 19.02
                                                             PROT
     ATOM
     ATOM
40
             100 N PRO 214
                               33.011 11.985 42.375 1.00 25.74
                                                              PROT
                                33.592 10.692 41.973 1.00 28.98
             101 CD PRO 214
                                                              PROT
     ATOM
                                32.145 12.536 41.322 1.00 23.38
     ATOM
            102 CA PRO 214
                                                              PROT
                                32.180 11.476 40.232 1.00 18.01
                                                              PROT
     ATOM
            103 CB PRO 214
     ATOM
            104 CG PRO 214
                                33.376 10.665 40.514 1.00 27.50
                                                              PROT
                               30.715 12.828 41.734 1.00 25.02
            105 C PRO 214
                                                              PROT
45
     ATOM
     ATOM
             106 O PRO 214
                               30.069 11.986 42.355 1.00 31.17
                                                              PROT
             107 N THR 215
                               30.211 14.009 41.377 1.00 19.56
     ATOM
                                                              PROT
                               28.830 14.352 41.714 1.00 24.48
            108 CA THR 215
                                                              PROT
     ATOM
     ATOM
             109 CB THR 215
                                28.535 15.841 41.522 1.00 27.13
                                                              PROT
            110 OG1 THR 215
                               27.939 16.038 40.234 1.00 40.19
                                                               PROT
50
     ATOM
```

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PROT
                               29.805 16.659 41.640 1.00 30.81
            111 CG2 THR 215
    ATOM
    ATOM
            112 C THR 215
                              27.899 13.562 40.805 1.00 22.14
                                                            PROT
            113 O THR 215
                              28.357 12.905 39.883 1.00 27.52
                                                            PROT
    ATOM
                              26.599 13.617 41.072 1.00 35.65
                                                            PROT
            114 N ASP 216
    ATOM
            115 CA ASP 216
                               25.631 12.890 40.258 1.00 41.16
                                                             PROT
    ATOM
            116 CB ASP 216
                              24.219 13.091 40.810 1.00 38.17
    ATOM
                                                             PROT
           117 C ASP 216
                              25.714 13.370 38.810 1.00 40.44
                                                            PROT
    ATOM
                              25.683 12.569 37.874 1.00 38.26
                                                            PROT
    ATOM 118 O ASP 216
                              25.832 14.682 38.635 1.00 40.14
                                                            PROT
    ATOM
            119 N GLU 217
            120 CA GLU 217
                               25.932 15.275 37.305 1.00 38.89
                                                            PROT
10
    ATOM
                               25.883 16.796 37.413 1.00 29.95
                                                             PROT
    ATOM 121 CB GLU 217
                              27.231 14.829 36.619 1.00 39.44
           122 C GLU 217
                                                             PROT
    ATOM
            123 O GLU 217
                              27.245 14.525 35.425 1.00 40.08
                                                             PROT
    ATOM
                              28.319 14.794 37.384 1.00 34.92
            124 N GLU 218
                                                             PROT
    ATOM
                               29.615 14.370 36.871 1.00 23.70
                                                             PROT
           125 CA GLU 218
15
    ATOM
    ATOM
            126 CB GLU 218
                               30.698 14.606 37.924 1.00 18.47
                                                             PROT
                               30.990 16.067 38.198 1.00 15.66
                                                             PROT
    ATOM 127 CG GLU 218
           128 CD GLU 218
                               32.085 16.264 39.231 1.00 26.88
                                                             PROT
    ATOM
                               32.164 15.458 40.191 1.00 25.07
                                                              PROT
    ATOM
           129 OE1 GLU 218
           130 OE2 GLU 218
                               32.864 17.232 39.078 1.00 33.79
                                                              PROT
20
    ATOM
                              29.589 12.892 36.491 1.00 21.05
           131 C GLU 218
                                                            PROT
    ATOM
           132 O GLU 218
                              30.182 12.490 35.495 1.00 24.30
                                                             PROT
    ATOM
    ATOM 133 N TRP 219
                              28.907 12.080 37.288 1.00 13.98
                                                            PROT
            134 CA TRP 219
                               28.829 10.660 37.000 1.00 17.30
                                                             PROT
    ATOM
            135 CB TRP 219
                               28.052 9.921 38.089 1.00 16.27
                                                            PROT
25
    ATOM
           136 CG TRP 219
                               28.890 9.520 39.277 1.00 31.14
    ATOM
                                                             PROT
                               29.984 8.585 39.296 1.00 36.40
                                                             PROT
           137 CD2 TRP 219
    ATOM
    ATOM 138 CE2 TRP 219
                               30.476 8.547 40.621 1.00 29.24
                                                             PROT
                               30.595 7.781 38.323 1.00 41.61
    ATOM
           139 CE3 TRP 219
                                                             PROT
            140 CD1 TRP 219
                               28.771 9.988 40.551 1.00 28.69
                                                             PROT
30
    ATOM
                               29.718 9.411 41.362 1.00 35.01
                                                             PROT
           141 NE1 TRP 219
    ATOM
                               31.552 7.737 41.004 1.00 30.89
                                                             PROT
    ATOM
            142 CZ2 TRP 219
                               31.673 6.969 38.707 1.00 45.72
                                                             PROT
    ATOM
            143 CZ3 TRP 219
                               32.137 6.958 40.038 1.00 35.17
            144 CH2 TRP 219
                                                             PROT
    ATOM
                              28.125 10.500 35.660 1.00 20.83
                                                            PROT
            145 C TRP 219
35
    ATOM
            146 O TRP 219
                              28.467 9.616 34.865 1.00 31.36
                                                            PROT
    ATOM
            147 N GLU 220
                              27.143 11.364 35.412 1.00 30.53
                                                             PROT
    ATOM
            148 CA GLU 220
                               26.400 11.323 34.159 1.00 33.95
                                                             PROT
    ATOM
    ATOM
            149 CB GLU 220
                               25.237 12.318 34.201 1.00 22.17
                                                             PROT
            150 C GLU 220
                              27.356 11.658 33.013 1.00 34.66
                                                             PROT
    ATOM
40
                              27.233 11.134 31.900 1.00 43.86
                                                             PROT
    ATOM
            151 O GLU 220
    ATOM
            152 N LEU 221
                              28.320 12.528 33.297 1.00 22.60
                                                             PROT
                               29.305 12.926 32.304 1.00 17.18
                                                             PROT
            153 CA LEU 221
    ATOM
                               29.995 14.219 32.743 1.00 11.03
                                                             PROT
            154 CB LEU 221
    ATOM
45
    ATOM
            155 CG LEU 221
                               31.078 14.824 31.850 1.00 5.17
                                                             PROT
            156 CD1 LEU 221
                               30.756 14.569 30.415 1.00 6.41
                                                             PROT
    ATOM
                                                            PROT
                               31.181 16.305 32.092 1.00 10.65
            157 CD2 LEU 221
    ATOM
    ATOM
            158 C LEU 221
                              30.344 11.817 32.122 1.00 22.25
                                                            PROT
            159 O LEU 221
                              30.759 11.521 31.002 1.00 18.99
                                                            PROT
    ATOM
                             30.754 11.198 33.228 1.00 20.74
                                                            PROT
50
    ATOM
            160 N ILE 222
```

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PROT
                             31.744 10.136 33.177 1.00 12.88
            161 CA ILE 222
    ATOM
                             32.115 9.662 34.587 1.00 12.96
           162 CB ILE 222
                                                          PROT
    ATOM
                              33.030 8.468 34.515 1.00 2.00
                                                          PROT
    ATOM 163 CG2 ILE 222
                              32.811 10.796 35.332 1.00 16.50
                                                          PROT
           164 CG1 ILE 222
    ATOM
    ATOM 165 CD1 ILE 222
                              33.625 10.351 36.511 1.00 15.90
                                                          PROT
5
                            31.241 8.958 32.363 1.00 17.72
                                                         PROT
    ATOM 166 C ILE 222
    ATOM 167 O ILE 222
                            32.001 8.363 31.594 1.00 16.59
                                                          PROT
                             29.966 8.618 32.530 1.00 33.88
                                                          PROT
    ATOM 168 N LYS 223
                              29.371 7.503 31.795 1.00 39.02
                                                          PROT
    ATOM 169 CA LYS 223
    ATOM 170 CB LYS 223
                              27.908 7.307 32.224 1.00 40.29
                                                           PROT
10
                             29.444 7.779 30.293 1.00 39.14
    ATOM 171 C LYS 223
                                                          PROT
                             29.949 6.963 29.517 1.00 32.99
    ATOM 172 O LYS 223
                                                          PROT
                             28.936 8.942 29.897 1.00 27.19
                                                          PROT
    ATOM 173 N THR 224
    ATOM 174 CA THR 224
                              28.929 9.363 28.498 1.00 25.75
                                                           PROT
                              28.440 10.817 28.407 1.00 22.51
                                                            PROT
    ATOM 175 CB THR 224
15
    ATOM 176 OG1 THR 224
                             27.018 10.837 28.568 1.00 35.46
                                                           PROT
                               28.799 11.436 27.083 1.00 15.53
                                                           PROT
           177 CG2 THR 224
    ATOM
           178 C THR 224
                             30.307 9.235 27.833 1.00 22.31
                                                          PROT
    ATOM
                             30.480 8.517 26.843 1.00 27.13
                                                           PROT
    ATOM 179 O THR 224
                              31.287 9.936 28.386 1.00 17.87
           180 N VAL 225
                                                           PROT
20
    ATOM
                             32.635 9.906 27.854 1.00 17.07
                                                           PROT
    ATOM
           181 CA VAL 225
    ATOM 182 CB VAL 225
                              33.559 10.759 28.720 1.00 16.86
                                                            PROT
           183 CG1 VAL 225
                               34.845 11.064 27.973 1.00 26.54
                                                           PROT
    ATOM
                               32.854 12.057 29.075 1.00 24.46
                                                           PROT
           184 CG2 VAL 225
    ATOM
    ATOM 185 C VAL 225
                             33.169 8.486 27.793 1.00 16.11
                                                          PROT
25
           186 O VAL 225
                                                           PROT
    ATOM
                              33.683 8.042 26.763 1.00 12.75
                             33.040 7.769 28.900 1.00 12.23
                                                           PROT
            187 N THR 226
    ATOM
                              33.520 6.400 28.951 1.00 12.34
                                                           PROT
    ATOM 188 CA THR 226
                              33.175 5.747 30.271 1.00 17.01
                                                           PROT
    ATOM
           189 CB THR 226
                               33.715 6.536 31.342 1.00 6.78
                                                           PROT
    ATOM
           190 OG1 THR 226
30
                               33.739 4.324 30.307 1.00 2.00
                                                           PROT
    ATOM 191 CG2 THR 226
                             32.909 5.581 27.837 1.00 14.82
                                                           PROT
    ATOM 192 C THR 226
                             33.623 4.953 27.061 1.00 20.90
                                                           PROT
    ATOM 193 O THR 226
                                                           PROT
    ATOM 194 N GLU 227
                              31.582 5.588 27.758 1.00 22.90
                              30.886 4.849 26.714 1.00 22.63
                                                           PROT
    ATOM 195 CA GLU 227
35
                                                           PROT
                              29.417 5.248 26.678 1.00 20.14
    ATOM 196 CB GLU 227
    ATOM 197 C GLU 227
                              31.556 5.173 25.386 1.00 21.74
                                                           PROT
                              32.057 4.283 24.700 1.00 24.42
                                                           PROT
    ATOM
           198 O GLU 227
                              31.590 6.460 25.050 1.00 13.26
                                                           PROT
    ATOM
           199 N ALA 228
                              32.196 6.928 23.800 1.00 22.76
                                                           PROT
            200 CA ALA 228
    ATOM
40
                              32.267 8.450 23.785 1.00 22.50
                                                           PROT
    ATOM
            201 CB ALA 228
                              33.584 6.358 23.538 1.00 19.19
    ATOM
            202 C ALA 228
                                                           PROT
            203 O ALA 228
                              33.913 6.003 22.408 1.00 17.19
                                                           PROT
    ATOM
                             34.408 6.290 24.573 1.00 20.11
                                                          PROT
            204 N HIS 229
    ATOM
45
    ATOM
            205 CA HIS 229
                              35.741 5.756 24.389 1.00 18.68
                                                           PROT
                              36.537 5.819 25.686 1.00 10.37
                                                           PROT
            206 CB HIS 229
    ATOM
            207 CG HIS 229
                              37.894 5.201 25.586 1.00 2.00
                                                          PROT
    ATOM
    ATOM
            208 CD2 HIS 229
                              38.524 4.299 26.376 1.00 7.61
                                                           PROT
                              38.780 5.517 24.582 1.00 3.78
                                                           PROT
    ATOM 209 ND1 HIS 229
                              39.900 4.837 24.758 1.00 15.67
                                                          PROT
50
    ATOM 210 CE1 HIS 229
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39.771 4.090 25.840 1.00 7.10
                                                          PROT
           211 NE2 HIS 229
    ATOM
           212 C HIS 229
                            35.637 4.316 23.940 1.00 21.45
                                                          PROT
    ATOM
                             36.127 3.950 22.866 1.00 22.42
                                                          PROT
    ATOM
           213 O HIS 229
                             34.983 3.505 24.762 1.00 21.64
                                                           PROT
           214 N VAL 230
    ATOM
           215 CA VAL 230
                              34.827 2.086 24.468 1.00 33.80
                                                           PROT
    ATOM
5
    ATOM 216 CB VAL 230
                              33.960 1.388 25.528 1.00 33.11
                                                           PROT
    ATOM 217 CG1 VAL 230
                             34.251 -0.106 25.515 1.00 33.80
                                                           PROT
                             34.228 1.985 26.896 1.00 26.54
                                                            PROT
    ATOM 218 CG2 VAL 230
    ATOM 219 C VAL 230
                             34.224 1.781 23.100 1.00 33.12
                                                           PROT
    ATOM 220 O VAL 230
                             34.703 0.897 22.385 1.00 40.80
                                                           PROT
10
    ATOM 221 N ALA 231
                             33.170 2.507 22.746 1.00 36.22
                                                           PROT
    ATOM 222 CA ALA 231
                              32.497 2.298 21.471 1.00 36.24
                                                           PROT
    ATOM 223 CB ALA 231
                            31.318 3.255 21.343 1.00 18.90
                                                           PROT
    ATOM 224 C ALA 231
                             33.445 2.501 20.303 1.00 37.54
                                                           PROT
                             33.342 1.816 19.285 1.00 35.93
    ATOM 225 O ALA 231
                                                           PROT
15
    ATOM 226 N THR 232
                             34.380 3.434 20.474 1.00 23.74
                                                           PROT
    ATOM 227 CA THR 232
                              35.329 3.789 19.432 1.00 15.54
                                                           PROT
    ATOM 228 CB THR 232
                              35.335 5.321 19.238 1.00 9.70
                                                           PROT
    ATOM 229 OG1 THR 232
                               35.733 5.949 20.460 1.00 16.73
                                                           PROT
    ATOM 230 CG2 THR 232
                              33.942 5.828 18.891 1.00 2.00
                                                           PROT
20
                             36.758 3.309 19.670 1.00 19.86
                                                          PROT
    ATOM 231 C THR 232
    ATOM 232 O THR 232
                             37.695 3.854 19.094 1.00 15.31
                                                           PROT
                              36,938 2.305 20.523 1.00 28.26
    ATOM 233 N ASN 233
                                                           PROT
                              38.280 1.771 20.772 1.00 39.32
                                                           PROT
    ATOM 234 CA ASN 233
    ATOM 235 CB ASN 233
                              38.435 1.343 22.234 1.00 47.14
                                                           PROT
25
    ATOM 236 CG ASN 233
                              39.804 1.689 22.801 1.00 54.02
                                                           PROT
                              40.633 2.303 22.128 1.00 60.36
                                                            PROT
    ATOM 237 OD1 ASN 233
    ATOM 238 ND2 ASN 233
                               40.045 1.296 24.045 1.00 48.67
                                                            PROT
                             38,507 0.574 19.840 1.00 49.33
    ATOM 239 C ASN 233
                                                           PROT
    ATOM 240 O ASN 233
                              38.338 0.693 18.625 1.00 65.36
                                                           PROT
30
                              38.877 -0.577 20.388 1.00 57.89
                                                           PROT
    ATOM 241 N ALA 234
    ATOM 242 CA ALA 234
                              39.090 -1.752 19.552 1.00 57.22
                                                           PROT
                             40.372 -1.595 18.754 1.00 48.03
                                                          PROT
    ATOM 243 CB ALA 234
    ATOM 244 C ALA 234
                             39.141 -3.027 20.384 1.00 62.42
                                                           PROT
    ATOM 245 O ALA 234
                              38.471 -3.073 21.440 1.00 56.93
                                                           PROT
35
    ATOM 246 OT ALA 234
                             39.853 -3.968 19.965 1.00 76.16
                                                          PROT
    ATOM 247 N TRP 239
                             41.987 -7.449 22.970 1.00 58.82
                                                           PROT
                              43.077 -6.886 22.154 1.00 51.37
                                                           PROT
    ATOM 248 CA TRP 239
    ATOM 249 CB TRP 239
                              43.325 -5.406 22.534 1.00 45.12
                                                           PROT
    ATOM 250 CG TRP 239
                              44.193 -5.170 23.760 1.00 43.09
                                                           PROT
40
    ATOM 251 CD2 TRP 239
                              45.617 -5.037 23.793 1.00 32.36
                                                            PROT
    ATOM 252 CE2 TRP 239
                              45.990 -4.872 25.142 1.00 28.37
                                                            PROT
                              46.615 -5.049 22.813 1.00 40.79
    ATOM 253 CE3 TRP 239
                                                            PROT
                              43.773 -5.073 25.059 1.00 46.63
    ATOM 254 CD1 TRP 239
                                                            PROT
45
    ATOM 255 NE1 TRP 239
                              44.847 -4.896 25.893 1.00 27.08
                                                            PROT
                              47.315 -4.717 25.535 1.00 35.48
    ATOM 256 CZ2 TRP 239
                                                            PROT
                              47.936 -4.896 23.204 1.00 40.18
    ATOM 257 CZ3 TRP 239
                                                            PROT
    ATOM 258 CH2 TRP 239
                              48.273 -4.733 24.554 1.00 49.93
                                                          PROT
                             44.422 -7.623 22.063 1.00 49.76
                                                          PROT
    ATOM 259 C TRP 239
                             44.944 -7.799 20.962 1.00 48.14
                                                           PROT
50
    ATOM 260 O TRP 239
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44.975 -8.048 23.198 1.00 38.92
                                                              PROT
             261 N LYS 240
     ATOM
                                46.263 -8.735 23.232 1.00 37.29
                                                              PROT
     ATOM
             262 CA LYS 240
             263 CB LYS 240
                                46.572 -9.196 24.657 1.00 38.79
                                                              PROT
     ATOM
     ATOM
            264 CG LYS 240
                                47.106 -8.099 25.571 1.00 38.43
                                                              PROT
                                48.307 -8.584 26.370 1.00 35.71
                                                              PROT
     ATOM
             265 CD LYS 240
 5
             266 CE LYS 240
                               48.631 -7.646 27.523 1.00 37.87
                                                              PROT
     ATOM
                                49.058 -8.377 28.750 1.00 28.85
                                                              PROT
     ATOM
            267 NZ LYS 240
                               46.404 -9.914 22.269 1.00 42.18
                                                              PROT
            268 C LYS 240
     ATOM
                               47.491 -10.132 21.732 1.00 45.89
                                                              PROT
            269 O LYS 240
     ATOM
                               45.331 -10.679 22.058 1.00 46.08
                                                              PROT
10
     ATOM
            270 N GLN 241
            271 CA GLN 241
                                45.390 -11.816 21.133 1.00 45.02
                                                               PROT
     ATOM
                                44.575 -13.011 21.638 1.00 46.30
                                                               PROT
             272 CB GLN 241
     ATOM
                                44.284 -13.018 23.116 1.00 60.38
                                                               PROT
     ATOM
            273 CG GLN 241
                                42.828 -13.312 23.408 1.00 63.76
                                                               PROT
     ATOM
            274 CD GLN 241
                                42.154 -13.988 22.631 1.00 66.34
                                                               PROT
     ATOM
            275 OE1 GLN 241
15
                                42.333 -12.801 24.531 1.00 69.18
                                                               PROT
            276 NE2 GLN 241
     ATOM
                               44.866 -11.405 19.764 1.00 45.77
             277 C GLN 241
                                                              PROT
     ATOM
                               45.107 -12.085 18.765 1.00 51.18
                                                              PROT
     ATOM
            278 O GLN 241
                               44.132 -10.300 19.723 1.00 42.04
                                                              PROT
            279 N LYS 242
     ATOM
                                                              PROT
20
            280 CA LYS 242
                                43.613 -9.794 18.464 1.00 48.33
     ATOM
            281 CB LYS 242
                                42.498 -8.786 18.727 1.00 40.17
                                                              PROT
     ATOM
            282 C LYS 242
                               44.796 -9.123 17.742 1.00 53.04
                                                             PROT
     ATOM
                                                              PROT
            283 O LYS 242
                               44.709 -8.753 16.565 1.00 48.21
     ATOM
            284 N ARG 243
                               45.906 -8.992 18.470 1.00 45.44
                                                              PROT
     ATOM
            285 CA ARG 243
                                47.128 -8.374 17.965 1.00 43.53
                                                               PROT
25
     ATOM
             286 CB ARG 243
                                48.108 -8.135 19.118 1.00 40.21
                                                               PROT
     ATOM
     ATOM
            287 C ARG 243
                               47.795 -9.220 16.892 1.00 45.96
                                                              PROT
                               47.684 -10.443 16.894 1.00 50.22
                                                              PROT
     ATOM
            288 O ARG 243
                               48.498 -8.551 15.982 1.00 52.12
                                                              PROT
             289 N LYS 244
     ATOM
30
     ATOM
            290 CA LYS 244
                                49.202 -9.202 14.879 1.00 45.30
                                                              PROT
                                48.466 -8.950 13.558 1.00 48.24
                                                              PROT
     ATOM
            291 CB LYS 244
                                47.109 -9.631 13.446 1.00 53.78
             292 CG LYS 244
                                                              PROT
     ATOM
                                46.835 -10.078 12.011 1.00 60.50
                                                               PROT
     ATOM
            293 CD LYS 244
                                46.038 -9.030 11.241 1.00 61.03
                                                              PROT
     ATOM
             294 CE LYS 244
                                45.455 -7.997 12.146 1.00 55.25
                                                              PROT
             295 NZ LYS 244
35
     ATOM
            296 C LYS 244
                               50.616 -8.641 14.786 1.00 40.33
                                                             PROT
     ATOM
            297 O LYS 244
                               50.849 -7.629 14.125 1.00 36.07
                                                              PROT
     ATOM
                               51,556 -9.312 15.445 1.00 27.87
                                                              PROT
     ATOM
            298 N PHE 245
                                52.949 -8.885 15.461 1.00 30.61
                                                              PROT
            299 CA PHE 245
     ATOM
40
     ATOM
             300 CB PHE 245
                                53.784 -9.887 16.253 1.00 20.28
                                                              PROT
                                53.454 -9.922 17.713 1.00 37.23
                                                              PROT
     ATOM
             301 CG PHE 245
             302 CD1 PHE 245
                                52.636 -10.917 18.234 1.00 40.93
                                                               PROT
     ATOM
                                                               PROT
             303 CD2 PHE 245
                                53.958 -8.959 18.577 1.00 41.60
     ATOM
                                52.326 -10.953 19.594 1.00 42.54
             304 CE1 PHE 245
                                                               PROT
     ATOM
             305 CE2 PHE 245
                                53.652 -8.989 19.936 1.00 45.84
                                                               PROT
45
     ATOM
                                52.835 -9.988 20.443 1.00 33.72
             306 CZ PHE 245
                                                              PROT
     ATOM
                               53.549 -8.693 14.068 1.00 38.75
                                                              PROT
             307 C PHE 245
     ATOM
             308 O PHE 245
                               53.794 -9.660 13.337 1.00 48.93
                                                              PROT
     ATOM
     ATOM
             309 N LEU 246
                               53.789 -7.437 13.704 1.00 41.18
                                                              PROT
                              54.362 -7.124 12.404 1.00 43.43
                                                              PROT
             310 CA LEU 246
50
     ATOM
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PROT
                               54.378 -5.612 12.181 1.00 42.78
            311 CB LEU 246
    ATOM
    ATOM
            312 CG LEU 246
                               54.535 -5.200 10.718 1.00 49.88
                                                              PROT
                                53.528 -4.113 10.365 1.00 40.64
                                                              PROT
    ATOM
            313 CD1 LEU 246
                                55.966 -4.730 10.485 1.00 48.66
                                                              PROT
            314 CD2 LEU 246
    ATOM
                              55.777 -7.692 12.250 1.00 42.60
            315 C LEU 246
                                                             PROT
    ATOM
5
                               56.677 -7.383 13.028 1.00 45.75
                                                             PROT
    ATOM
            316 O LEU 246
            317 N PRO 247
                               55.977 -8.540 11.233 1.00 50.03
                                                             PROT
    ATOM
                               54.914 -8.924 10.286 1.00 60.17
                                                             PROT
            318 CD PRO 247
    ATOM
                               57.237 -9.199 10.894 1.00 49.90
                                                              PROT
    ATOM
            319 CA PRO 247
            320 CB PRO 247
                               57.181 -9.282 9.369 1.00 59.51
                                                             PROT
10
    ATOM
                               55.678 -9.244 9.023 1.00 52.86
                                                             PROT
            321 CG PRO 247
    ATOM
            322 C PRO 247
                               58.499 -8.494 11.392 1.00 48.85
                                                             PROT
    ATOM
                               58.675 -7.295 11.186 1.00 49.28
                                                             PROT
    ATOM
            323 O PRO 247
                                                             PROT
            324 N GLU 248
                               59.379 -9.261 12.032 1.00 47.62
    ATOM
                                                              PROT
            325 CA GLU 248
                                60.628 -8.733 12.574 1.00 51.41
15
    ATOM
                                                              PROT
            326 CB GLU 248
                                61,266 -9.750 13,522 1.00 44,22
    ATOM
            327 C GLU 248
                               61.623 -8.354 11.490 1.00 53.28
                                                             PROT
    ATOM
            328 O GLU 248
                               62.815 -8.214 11.765 1.00 62.57
                                                             PROT
    ATOM
                                                             PROT
     ATOM
            329 N ASP 249
                               61.146 -8.200 10.258 1.00 56.20
                               62.030 -7.818 9.164 1.00 55.88
                                                             PROT
            330 CA ASP 249
20
     ATOM
                                                             PROT
            331 CB ASP 249
                               62.231 -8.981 8.173 1.00 53.88
    ATOM
            332 CG ASP 249
                               60.928 -9.637 7.739 1.00 54.39
                                                             PROT
    ATOM
            333 OD1 ASP 249
                                60.578 -10.693 8.310 1.00 57.70
                                                              PROT
     ATOM
                                60.264 -9.112 6.819 1.00 45.76
                                                              PROT
            334 OD2 ASP 249
     ATOM
                              61.539 -6.567 8.437 1.00 54.20
                                                            PROT
25
     ATOM
            335 C ASP 249
                              62.119 -6.154 7.429 1.00 55.31
                                                            PROT
     ATOM
            336 O ASP 249
                              60.469 -5.965 8.954 1.00 46.13
                                                            PROT
            337 N ILE 250
     ATOM
                               59.933 -4.735 8.376 1.00 46.12
                                                             PROT
     ATOM
            338 CA ILE 250
            339 CB ILE 250
                               58.413 -4.764 8.253 1.00 43.38
                                                             PROT
     ATOM
            340 CG2 ILE 250
                               57.892 -3.344 8.057 1.00 39.15
                                                             PROT
30
     ATOM
                               58.007 -5.654 7.074 1.00 48.96
                                                             PROT
            341 CG1 ILE 250
     ATOM
                               56.707 -6.401 7.283 1.00 43.14
                                                             PROT
            342 CD1 ILE 250
     ATOM
                              60.311 -3.590 9.294 1.00 45.32
                                                            PROT
     ATOM
            343 C ILE 250
                              60.257 -3.724 10.513 1.00 43.74
            344 O ILE 250
                                                            PROT
     ATOM
                               60.680 -2.459 8.711 1.00 36.80
                                                             PROT
            345 N GLY 251
35
     ATOM
            346 CA GLY 251
                                61.091 -1.329 9.521 1.00 39.28
                                                              PROT
     ATOM
                                                             PROT
            347 C GLY 251
                               62.370 -1.621 10.305 1.00 44.31
     ATOM
            348 O GLY 251
                               62.538 -1.145 11.428 1.00 51.39
                                                             PROT
     ATOM
                                                             PROT
     ATOM
            349 N GLN 252
                               63.277 -2.399 9.715 1.00 55.47
                                64.536 -2.745 10.374 1.00 54.24
                                                              PROT
            350 CA GLN 252
40
     ATOM
                                64.792 -4.237 10.245 1.00 49.31
                                                              PROT
            351 CB GLN 252
     ATOM
                                                             PROT
     ATOM
            352 C GLN 252
                               65.720 -1.959 9.812 1.00 54.86
            353 O GLN 252
                               65.492 -1.079 8.953 1.00 58.80
                                                             PROT
     ATOM
                                60.887 6.759 5.510 1.00 34.33
                                                              PROT
            354 CB VAL 264
     ATOM
45
     ATOM
            355 CG1 VAL 264
                                59.550 6.086 5.790 1.00 34.34
                                                              PROT
                                60.893 8.163 6.080 1.00 20.22
                                                              PROT
            356 CG2 VAL 264
     ATOM
                               62.053 4.557 5.439 1.00 34.08
                                                             PROT
            357 C VAL 264
     ATOM
     ATOM
            358 O VAL 264
                               62.280 4.466 4.232 1.00 46.39
                                                             PROT
            359 N VAL 264
                               63.361 6.605 5.966 1.00 21.27
                                                             PROT
     ATOM
                               62.041 5.920 6.122 1.00 29.68
                                                              PROT
50
     ATOM
            360 CA VAL 264
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61.809 3.499 6.209 1.00 40.63
                                                          PROT
            361 N ASP 265
     ATOM
                                                           PROT
    ATOM
            362 CA ASP 265
                              61.796 2.141 5.670 1.00 43.58
                              61.243 1.160 6.704 1.00 44.07
                                                           PROT
    ATOM
            363 CB ASP 265
           364 CG ASP 265
                              61.179 -0.262 6.185 1.00 49.19
                                                           PROT
    ATOM
            365 OD1 ASP 265
                               62.223 -0.945 6.175 1.00 57.67
                                                           PROT
5
    ATOM
                               60.082 -0.702 5.789 1.00 54.75
            366 OD2 ASP 265
    ATOM
                                                          PROT
            367 C ASP 265
                             60.956 2.071 4.401 1.00 48.03
                                                          PROT
    ATOM
           368 O ASP 265
                             61.362 1.458 3.411 1.00 57.44
                                                          PROT
    ATOM
                              59.793 2.711 4.436 1.00 40.55
            369 N LEU 266
    ATOM
                                                          PROT
10
    ATOM
            370 CA LEU 266
                              58.879 2.741 3.295 1.00 45.78
                                                           PROT
                              59.638 2.962 1.977 1.00 45.92
    ATOM
           371 CB LEU 266
                                                           PROT
            372 CG LEU 266
                              59.881 4.407 1.506 1.00 48.41
                                                           PROT
    ATOM
           373 CD1 LEU 266
                              59.934 4.432 -0.007 1.00 32.83
                                                           PROT
    ATOM
           374 CD2 LEU 266
    ATOM
                               58.787 5.344 2.012 1.00 45.08
                                                          PROT
                             58.064 1.462 3.214 1.00 45.45
           375 C LEU 266
                                                          PROT
15
    ATOM
    ATOM
           376 O LEU 266
                              56.862 1.503 2.949 1.00 42.92
                                                          PROT
            377 N GLU 267
                              58.712 0.324 3.431 1.00 46.47
                                                          PROT
    ATOM
    ATOM
           378 CA GLU 267
                              57.986 -0.935 3.415 1.00 44.34
                                                           PROT
           379 CB GLU 267
                              58.943 -2.123 3.505 1.00 39.42
    ATOM
                                                           PROT
           380 CG GLU 267
                               58.291 -3.457 3.188 1.00 40.68
20
                                                           PROT
    ATOM
           381 CD GLU 267
                               58.929 -4.607 3.943 1.00 63.54
                                                           PROT
    ATOM
    ATOM
            382 OE1 GLU 267
                               60.103 -4.470 4.361 1.00 68.92
                                                           PROT
            383 OE2 GLU 267
                               58.258 -5.650 4.120 1.00 66.66
                                                          PROT
    ATOM
           384 C GLU 267
                              57.106 -0.880 4.655 1.00 41.57
                                                           PROT
    ATOM
           385 O GLU 267
                              55.991 -1.398 4.673 1.00 48.68
                                                           PROT
25
    ATOM
           386 N ALA 268
                                                           PROT
    ATOM
                              57.620 -0.215 5.686 1.00 39.33
           387 CA ALA 268
                             56.916 -0.057 6.951 1.00 31.62
                                                          PROT
    ATOM
            388 CB ALA 268 57.918 0.134 8.063 1.00 7.56
                                                           PROT
    ATOM
            389 C ALA 268
                              55.960 1.135 6.888 1.00 25.96
    ATOM
                                                          PROT
            390 O ALA 268
                              54.786 1.036 7.237 1.00 17.35
                                                          PROT
30
    ATOM
           391 N PHE 269
                             56.464 2.274 6.446 1.00 11.34
                                                          PROT
    ATOM
                              55.615 3.453 6.335 1.00 15.72
           392 CA PHE 269
                                                           PROT
    ATOM
           393 CB PHE 269
                              56.274 4.474 5.405 1.00 20.08
                                                           PROT
    ATOM
                              55.552 5.788 5.334 1.00 24.67
    ATOM
           394 CG PHE 269
                                                           PROT
           395 CD1 PHE 269
                               55.661 6.713 6.369 1.00 15.69
    ATOM
                                                           PROT
35
    ATOM
           396 CD2 PHE 269
                               54.772 6.111 4.222 1.00 20.64
                                                           PROT
    ATOM 397 CE1 PHE 269
                               55.003 7.942 6.300 1.00 22.55
                                                           PROT
                              54.108 7.342 4.143 1.00 19.77
    ATOM
           398 CE2 PHE 269
                                                           PROT
                              54.224 8.257 5.186 1.00 19.27
    ATOM
           399 CZ PHE 269
                                                           PROT
           400 C PHE 269
                             54.277 3.010 5.754 1.00 19.45
                                                          PROT
40
    ATOM
                             53.212 3.351 6.261 1.00 13.40
                                                          PROT
    ATOM
           401 O PHE 269
    ATOM
           402 N SER 270
                             54.367 2.214 4.692 1.00 43.85
                                                          PROT
            403 CA SER 270
                              53.217 1.686 3.967 1.00 46.67
                                                          PROT
    ATOM
           404 CB SER 270
                              53.687 0.669 2.924 1.00 53.60
                                                           PROT
    ATOM
45
    ATOM
           405 OG SER 270
                             52.662 0.382 1.988 1.00 68.82
                                                           PROT
            406 C SER 270
                             52.181 1.039 4.865 1.00 43.32
                                                          PROT
    ATOM
            407 O SER 270
                             51.024 1.459 4.893 1.00 43.87
                                                          PROT
    ATOM
    ATOM
           408 N HIS 271
                             52.594 0.009 5.590 1.00 34.59
                                                          PROT
           409 CA HIS 271
                            51.681 -0.694 6.486 1.00 37.12
                                                          PROT
    ATOM
                            52.441 -1.772 7.266 1.00 46.61
           410 CB HIS 271
                                                          PROT
50
    ATOM
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52.603 -3.056 6.512 1.00 63.99
                                                           PROT
    ATOM
            411 CG HIS 271
                              51.879 -4.201 6.533 1.00 62.06
            412 CD2 HIS 271
                                                           PROT
    ATOM
            413 ND1 HIS 271
                              53.608 -3.256 5.590 1.00 60.86
                                                           PROT
    ATOM
            414 CE1 HIS 271
                              53.497 -4.467 5.075 1.00 60.70
    ATOM
                                                           PROT
                              52.456 -5.061 5.630 1.00 64.10
                                                           PROT
5
    ATOM
            415 NE2 HIS 271
                             50.973 0.261 7.459 1.00 36.53
                                                          PROT
            416 C HIS 271
    ATOM
                             49.744 0.245 7.586 1.00 37.75
                                                          PROT
    ATOM
            417 O HIS 271
                             51.752 1.099 8.133 1.00 32.81
                                                          PROT
    ATOM
            418 N PHE 272
           419 CA PHE 272
                              51.190 2.038 9.085 1.00 27.77
                                                           PROT
    ATOM
                              52.302 2.886 9.714 1.00 10.49
                                                           PROT
10
    ATOM
           420 CB PHE 272
                              53.338 2.086 10.459 1.00 6.98
           421 CG PHE 272
                                                           PROT
    ATOM
                               54.671 2.478 10.449 1.00 4.13
           422 CD1 PHE 272
                                                           PROT
    ATOM
                               52.978 0.961 11.193 1.00 6.95
                                                           PROT
    ATOM
            423 CD2 PHE 272
                               55.634 1.764 11.163 1.00 7.86
                                                           PROT
    ATOM
            424 CE1 PHE 272
                                                           PROT
           425 CE2 PHE 272
                              53.930 0.242 11.909 1.00 6.13
    ATOM
15
                              55.263 0.645 11.895 1.00 8.93
                                                           PROT
            426 CZ PHE 272
    ATOM
           427 C PHE 272
                             50.168 2.939 8.405 1.00 30.96
                                                          PROT
    ATOM
                             49.071 3.156 8.931 1.00 30.21
           428 O PHE 272
                                                          PROT
    ATOM
                              50.522 3.452 7.231 1.00 31.55
                                                          PROT
           429 N THR 273
    ATOM
                              49.633 4.343 6.487 1.00 33.39
                                                           PROT
20
    ATOM
           430 CA THR 273
                              50.335 4.912 5.243 1.00 36.80
                                                           PROT
           431 CB THR 273
    ATOM
           432 OG1 THR 273
                               50,649 3.847 4.332 1.00 27.42
                                                           PROT
    ATOM
                               51.613 5.641 5.656 1.00 32.25
                                                            PROT
    ATOM 433 CG2 THR 273
           434 C THR 273
                             48.350 3.647 6.056 1.00 34.07
                                                          PROT
    ATOM
                              47.362 4.294 5.697 1.00 17.11
                                                           PROT
25
    ATOM
            435 O THR 273
           436 N LYS 274
                             48.372 2.321 6.088 1.00 34.47
                                                          PROT
    ATOM
                              47.196 1.555 5.726 1.00 42.17
                                                           PROT
    ATOM
           437 CA LYS 274
                              47.544 0.069 5.615 1.00 40.02
                                                           PROT
            438 CB LYS 274
    ATOM
            439 C LYS 274
                             46.153 1.778 6.818 1.00 41.47
                                                          PROT
    ATOM
30
    ATOM
            440 O LYS 274
                             45.115 2.402 6.584 1.00 47.37
                                                          PROT
                             46.456 1.290 8.019 1.00 34.08
                                                          PROT
    ATOM
            441 N ILE 275
            442 CA ILE 275
                             45.559 1.403 9.166 1.00 25.49
                                                          PROT
    ATOM
                             45.991 0.435 10.262 1.00 19.72
                                                           PROT
    ATOM
            443 CB ILE 275
                              46.290 -0.934 9.642 1.00 23.39
                                                           PROT
    ATOM
            444 CG2 ILE 275
            445 CG1 ILE 275
                              47.249 0.958 10.953 1.00 12.96
                                                           PROT
    ATOM
35
                              47.970 -0.103 11.769 1.00 11.07
                                                           PROT
    ATOM
            446 CD1 ILE 275
            447 C ILE 275
                             45.440 2.805 9.762 1.00 20.03
                                                          PROT
    ATOM
            448 O ILE 275
                             44.541 3.081 10.547 1.00 18.98
                                                          PROT
    ATOM
                             46.347 3.694 9.402 1.00 8.88
                                                         PROT
            449 N ILE 276
    ATOM
    ATOM
            450 CA ILE 276
                             46.268 5.043 9.924 1.00 6.62
                                                          PROT
40
                             47.298 5.972 9.261 1.00 21.77
                                                          PROT
            451 CB ILE 276
    ATOM
            452 CG2 ILE 276
                              46.894 6.267 7.831 1.00 27.28
                                                           PROT
    ATOM
            453 CG1 ILE 276
                              47.374 7.288 10.028 1.00 6.75
                                                           PROT
    ATOM
                              48.349 7.255 11.153 1.00 15.44
                                                          PROT
            454 CD1 ILE 276
    ATOM
                             44.887 5.649 9.697 1.00 12.17
                                                          PROT
45
    ATOM
            455 C ILE 276
            456 O ILE 276
                             44.349 6.331 10.565 1.00 29.36
                                                          PROT
    ATOM
                              44.303 5.411 8.535 1.00 22.12
                                                           PROT
            457 N THR 277
    ATOM
            458 CA THR 277 43.007 6.005 8.260 1.00 27.16
                                                          PROT
    ATOM
    ATOM
            459 CB THR 277
                              42.532 5.675 6.834 1.00 27.11
                                                           PROT
            460 OG1 THR 277 43.665 5.584 5.955 1.00 22.55
                                                          PROT
50
    ATOM
```

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PROT
                               41.594 6.763 6.337 1.00 26.98
    ATOM
            461 CG2 THR 277
                              41.944 5.591 9.270 1.00 25.23
            462 C THR 277
                                                           PROT
    ATOM
                                                           PROT
    ATOM
            463 O THR 277
                              41.271 6.443 9.847 1.00 21.62
                              41.769 4.279 9.491 1.00 18.64
                                                           PROT
            464 N PRO 278
    ATOM
                               42.472 3.167 8.832 1.00 9.52
                                                            PROT
            465 CD PRO 278
    ATOM
    ATOM
            466 CA PRO 278
                               40.765 3.803 10.453 1.00 18.48
                                                             PROT
                               40.907 2.280 10.415 1.00 14.77
                                                             PROT
            467 CB PRO 278
    ATOM
            468 CG PRO 278
                               42.195 2.008 9.738 1.00 7.70
                                                            PROT
    ATOM
                              40.956 4.356 11.870 1.00 25.40
    ATOM
            469 C PRO 278
                                                            PROT
            470 O PRO 278
                              39.983 4.628 12.576 1.00 22.33
                                                            PROT
10
    ATOM
            471 N ALA 279
                              42.211 4.507 12.285 1.00 22.14
                                                            PROT
    ATOM
                               42.519 5.038 13.607 1.00 20.26
                                                             PROT
    ATOM
            472 CA ALA 279
                              44.016 5.033 13.831 1.00 13.33
                                                             PROT
    ATOM
            473 CB ALA 279
                              41.984 6.456 13.699 1.00 16.49
            474 C ALA 279
                                                            PROT
    ATOM
                              41.222 6.797 14.598 1.00 32.38
                                                            PROT
            475 O ALA 279
15
    ATOM
            476 N ILE 280
                             42.384 7.286 12.753 1.00 7.56
                                                           PROT
    ATOM
                              41.935 8.666 12.734 1.00 9.96
                                                           PROT
    ATOM
            477 CA ILE 280
                              42.422 9.380 11.462 1.00 8.46
                                                           PROT
            478 CB ILE 280
     ATOM
            479 CG2 ILE 280
                              42.172 10.871 11.581 1.00 2.00
                                                            PROT
    ATOM
                              43.901 9.059 11.220 1.00 10.96
            480 CG1 ILE 280
                                                            PROT
20
    ATOM
                               44,615 10.036 10.294 1.00 8.54
                                                            PROT
    ATOM
            481 CD1 ILE 280
            482 C ILE 280
                             40.410 8.805 12.805 1.00 15.46
                                                           PROT
    ATOM
            483 O ILE 280
                             39.887 9.741 13.421 1.00 24.39
                                                           PROT
    ATOM
                              39.692 7.883 12.172 1.00 24.18
                                                            PROT
            484 N THR 281
    ATOM
                               38.238 7.962 12.153 1.00 24.77
                                                             PROT
25
    ATOM
            485 CA THR 281
    ATOM
            486 CB THR 281
                               37.650 6.952 11.145 1.00 33.90
                                                             PROT
                               38.607 6.711 10.108 1.00 34.62
                                                             PROT
            487 OG1 THR 281
    ATOM
                               36.379 7.506 10.513 1.00 39.80
                                                            PROT
            488 CG2 THR 281
    ATOM
    ATOM
            489 C THR 281
                              37.655 7.726 13.535 1.00 23.39
                                                            PROT
                              36.733 8.422 13.960 1.00 19.51
                                                            PROT
            490 O THR 281
30
    ATOM
                              38.213 6.743 14.234 1.00 16.90
                                                            PROT
            491 N ARG 282
     ATOM
                               37.781 6.404 15.583 1.00 12.29
                                                             PROT
    ATOM
            492 CA ARG 282
                               38.641 5.260 16.115 1.00 5.36
                                                            PROT
    ATOM
            493 CB ARG 282
            494 CG ARG 282
                               37.936 3.926 16.136 1.00 17.05
                                                             PROT
     ATOM
                               38.296 3.095 14.942 1.00 18.41
                                                             PROT
35
    ATOM
            495 CD ARG 282
                               39.622 2.475 15.011 1.00 35.77
                                                             PROT
    ATOM
            496 NE ARG 282
                               40.454 2.501 16.055 1.00 36.80
                                                             PROT
            497 CZ ARG 282
     ATOM
                                41.629 1.888 15.967 1.00 35.96
                                                              PROT
            498 NH1 ARG 282
     ATOM
                                40.134 3.120 17.183 1.00 25.20
     ATOM
            499 NH2 ARG 282
                                                              PROT
                              37.863 7.626 16.520 1.00 16.75
                                                            PROT
            500 C ARG 282
40
     ATOM
            501 O ARG 282
                               37.078 7.758 17.456 1.00 22.98
                                                            PROT
     ATOM
     ATOM
            502 N VAL 283
                              38.813 8.518 16.268 1.00 11.92
                                                            PROT
            503 CA VAL 283
                               38.937 9.719 17.083 1.00 14.68
                                                             PROT
     ATOM
                                                             PROT
                               40.191 10.541 16.696 1.00 23.35
     ATOM
            504 CB VAL 283
                                40.467 11.593 17.752 1.00 11.98
45
     ATOM
            505 CG1 VAL 283
                                                              PROT
            506 CG2 VAL 283
                                41.396 9.621 16.526 1.00 20.41
                                                             PROT
     ATOM
                              37.705 10.580 16.833 1.00 12.72
                                                             PROT
     ATOM
            507 C VAL 283
            508 O VAL 283
                              36.965 10.929 17.752 1.00 20.37
                                                             PROT
     ATOM
            509 N VAL 284
                              37.503 10.920 15.567 1.00 18.28
                                                             PROT
     ATOM
                              36.369 11.727 15.150 1.00 16.98
                                                             PROT
50
            510 CA VAL 284
     ATOM
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36.251 11.765 13.602 1.00 27.40
                                                             PROT
    ATOM
            511 CB VAL 284
            512 CG1 VAL 284
                                35.434 12.973 13.172 1.00 19.30
                                                             PROT
    ATOM
           513 CG2 VAL 284
                                37.649 11.794 12.959 1.00 16.94
                                                              PROT
    ATOM
                              35.113 11.093 15.715 1.00 14.89
                                                             PROT
            514 C VAL 284
    ATOM
            515 O VAL 284
                              34.233 11.781 16.219 1.00 10.93
                                                             PROT
    ATOM
            516 N ASP 285
                              35.046 9.768 15.623 1.00 10.68
                                                            PROT
    ATOM
                               33.898 9.022 16.114 1.00 20.76
                                                             PROT
            517 CA ASP 285
    ATOM
                               34.079 7.518 15.874 1.00 22.99
            518 CB ASP 285
                                                             PROT
    ATOM
                               33.985 7.130 14.397 1.00 30.01
    ATOM
            519 CG ASP 285
                                                             PROT
                               33.185 7.735 13.648 1.00 18.56
            520 OD1 ASP 285
                                                             PROT
10
    ATOM
            521 OD2 ASP 285
                               34.720 6.202 13.993 1.00 27.74
                                                             PROT
    ATOM
            522 C ASP 285
                              33.734 9.274 17.604 1.00 26.87
                                                            PROT
    ATOM
    ATOM
            523 O ASP 285
                              32.609 9.349 18.103 1.00 39.89
                                                            PROT
                              34.861 9.405 18.308 1.00 25.45
            524 N PHE 286
                                                            PROT
    ATOM
                               34.862 9.654 19.746 1.00 15.66
                                                             PROT
            525 CA PHE 286
15
    ATOM
                               36.284 9.533 20.305 1.00 7.30
                                                            PROT
            526 CB PHE 286
    ATOM
            527 CG PHE 286
                               36.454 10.104 21.703 1.00 17.92
                                                             PROT
    ATOM
                               35.848 9.499 22.805 1.00 19.35
                                                             PROT
    ATOM
           528 CD1 PHE 286
            529 CD2 PHE 286
                               37.229 11.245 21.920 1.00 19.24
                                                              PROT
    ATOM
                               36.014 10.021 24.087 1.00 9.94
            530 CE1 PHE 286
                                                             PROT
20
    ATOM
            531 CE2 PHE 286
                               37.395 11.769 23.207 1.00 11.33
                                                             PROT
    ATOM
                               36.786 11.154 24.283 1.00 2.00
            532 CZ PHE 286
                                                             PROT
    ATOM
                              34.313 11.043 20.030 1.00 17.67
           533 C PHE 286
                                                            PROT
    ATOM
                              33.367 11.201 20.797 1.00 14.36
            534 O PHE 286
                                                            PROT
    ATOM
25
    ATOM
            535 N ALA 287
                              34.905 12.056 19.410 1.00 12.57
                                                             PROT
            536 CA ALA 287
                               34.443 13.426 19.622 1.00 12.49
                                                             PROT
    ATOM
            537 CB ALA 287
                               35.250 14.386 18.759 1.00 23.54
                                                             PROT
    ATOM
            538 C ALA 287
                              32.954 13.559 19.307 1.00 9.21
                                                            PROT
     ATOM
     ATOM
            539 O ALA 287
                              32.209 14.205 20.043 1.00 11.68
                                                             PROT
                              32.540 12.929 18.209 1.00 16.43
                                                            PROT
     ATOM
            540 N LYS 288
30
                               31.157 12.944 17.736 1.00 16.10
                                                             PROT
            541 CA LYS 288
     ATOM
            542 CB LYS 288
                               31.003 11.977 16.569 1.00 13.15
                                                             PROT
    ATOM
    ATOM
            543 CG LYS 288
                               31.117 12.636 15.219 1.00 25.55
                                                             PROT
                               30.480 11.779 14.136 1.00 32.95
                                                             PROT
            544 CD LYS 288
     ATOM
                               31.279 10.507 13.900 1.00 34.58
     ATOM
            545 CE LYS 288
                                                             PROT
35
            546 NZ LYS 288
                               30.755 9.721 12.748 1.00 36.93
                                                             PROT
     ATOM
           547 C LYS 288
                              30.154 12.569 18.813 1.00 18.87
                                                            PROT
     ATOM
                              29.078 13.171 18.917 1.00 12.83
                                                             PROT
    ATOM
            548 O LYS 288
            549 N LYS 289
                              30.525 11.574 19.614 1.00 11.81
                                                             PROT
     ATOM
                               29.674 11.067 20.681 1.00 15.53
                                                             PROT
40
     ATOM
           550 CA LYS 289
                               30.070 9.631 21.011 1.00 15.88
                                                             PROT
     ATOM
            551 CB LYS 289
     ATOM
            552 CG LYS 289
                               29.767 8.645 19.911 1.00 20.93
                                                             PROT
            553 CD LYS 289
                               29.140 7.382 20.471 1.00 28.97
                                                             PROT
     ATOM
     ATOM
            554 CE LYS 289
                               29.951 6.167 20.071 1.00 25.06
                                                             PROT
            555 NZ LYS 289
                               30.043 6.060 18.590 1.00 39.19
                                                             PROT
45
     ATOM
            556 C LYS 289
                              29.660 11.884 21.969 1.00 15.95
                                                            PROT
     ATOM
                              29.205 11.398 23.001 1.00 28.53
     ATOM
            557 O LYS 289
                                                             PROT
            558 N LEU 290
                              30.151 13.116 21.919 1.00 10.13
                                                             PROT
     ATOM
                              30.155 13.959 23.104 1.00 7.83
            559 CA LEU 290
                                                             PROT
     ATOM
                               31.588 14.300 23.532 1.00 14.46
                                                             PROT
50
     ATOM
            560 CB LEU 290
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PROT
            561 CG LEU 290
                               32.676 13.228 23.542 1.00 11.22
     ATOM
                               34.016 13.900 23.678 1.00 3.02
                                                             PROT
     ATOM
            562 CD1 LEU 290
                               32.449 12.257 24.686 1.00 9.39
                                                             PROT
            563 CD2 LEU 290
     ATOM
     ATOM
            564 C LEU 290
                              29.410 15.259 22.849 1.00 7.59
                                                            PROT
                              29.942 16.148 22.196 1.00 11.01
                                                             PROT
            565 O LEU 290
 5
     ATOM
                              28.169 15.381 23.365 1.00 14.33
                                                             PROT
            566 N PRO 291
     ATOM
           567 CD PRO 291
                               27.515 14.291 24.109 1.00 18.52
                                                             PROT
     ATOM
            568 CA PRO 291
                               27.290 16.556 23.240 1.00 6.61
                                                             PROT
     ATOM
                               26.296 16.400 24.384 1.00 11.95
                                                             PROT
            569 CB PRO 291
     ATOM
                               26.496 15.004 24.929 1.00 20.22
                                                             PROT
10
     ATOM
            570 CG PRO 291
                              28.029 17.885 23.332 1.00 14.74
                                                             PROT
            571 C PRO 291
     ATOM
                              27.795 18.792 22.537 1.00 26.09
                                                             PROT
            572 O PRO 291
     ATOM
                               28.917 18.002 24.315 1.00 24.06
                                                             PROT
            573 N MET 292
     ATOM
            574 CA MET 292
                               29.697 19.225 24.494 1.00 25.33
                                                              PROT
     ATOM
            575 CB MET 292
                               30.706 19.046 25.628 1.00 26.65
                                                              PROT
15
     ATOM
                               30.222 19.581 26.962 1.00 26.97
                                                              PROT
           576 CG MET 292
     ATOM
                               31.153 18.943 28.362 1.00 29.01
                                                              PROT
           577 SD MET 292
     ATOM
                               30.315 17.438 28.685 1.00 17.91
                                                             PROT
           578 CE MET 292
     ATOM
                               30.430 19.588 23.204 1.00 23.01
           579 C MET 292
                                                             PROT
     ATOM
                               30.478 20.747 22.813 1.00 31.98
                                                             PROT
20
     ATOM
           580 O MET 292
                              31.007 18.591 22.547 1.00 23.44
           581 N PHE 293
                                                             PROT
     ATOM
                               31.724 18.819 21.297 1.00 24.83
     ATOM 582 CA PHE 293
                                                             PROT
     ATOM 583 CB PHE 293
                               32.389 17.529 20.830 1.00 15.05
                                                             PROT
     ATOM 584 CG PHE 293
                               33.214 17.686 19.594 1.00 13.55
                                                             PROT
                                                              PROT
     ATOM 585 CD1 PHE 293
                               34.376 18.446 19.614 1.00 19.86
25
                                32.867 17.024 18.425 1.00 22.99
                                                              PROT
     ATOM 586 CD2 PHE 293
                                                              PROT
     ATOM 587 CE1 PHE 293
                               35.184 18.540 18.495 1.00 18.15
                               33.671 17.108 17.291 1.00 20.83
                                                              PROT
     ATOM 588 CE2 PHE 293
                               34.831 17.866 17.328 1.00 22.53
                                                             PROT
     ATOM 589 CZ PHE 293
                              30.759 19.291 20.222 1.00 27.26
                                                             PROT
            590 C PHE 293
30
     ATOM
                              30.971 20.319 19.577 1.00 28.69
                                                             PROT
            591 O PHE 293
     ATOM
                              29.689 18.528 20.040 1.00 29.92
                                                             PROT
            592 N CYS 294
     ATOM
                               28.700 18.855 19.037 1.00 35.54
                                                             PROT
            593 CA CYS 294
     ATOM
            594 CB CYS 294
                               27.540 17.860 19.106 1.00 19.11
                                                             PROT
     ATOM
                                                             PROT
            595 SG CYS 294
                               27.843 16.358 18.132 1.00 35.66
35
     ATOM
                              28.203 20.291 19.171 1.00 38.84
                                                             PROT
            596 C CYS 294
     ATOM
     ATOM 597 O CYS 294
                              28.072 20.995 18.169 1.00 45.94
                                                             PROT
     ATOM 598 N GLU 295
                               27.959 20.739 20.401 1.00 27.34
                                                             PROT
                               27.472 22.097 20.632 1.00 21.06
                                                              PROT
     ATOM 599 CA GLU 295
                               27.178 22.306 22.121 1.00 29.78
                                                              PROT
     ATOM 600 CB GLU 295
40
                               28.458 23.158 20.128 1.00 23.67
                                                             PROT
     ATOM 601 C GLU 295
                               28.228 24.357 20.272 1.00 29.89
                                                             PROT
     ATOM 602 O GLU 295
     ATOM 603 N LEU 296
                               29.551 22.715 19.522 1.00 21.46
                                                             PROT
                               30.545 23.642 19.005 1.00 26.35
                                                              PROT
     ATOM 604 CA LEU 296
                               31.947 23.128 19.330 1.00 25.17
                                                             PROT
     ATOM 605 CB LEU 296
45
     ATOM 606 CG LEU 296
                               32.419 23.157 20.778 1.00 13.78
                                                              PROT
                                33.593 22.217 20.931 1.00 23.61
                                                              PROT
            607 CD1 LEU 296
     ATOM
            608 CD2 LEU 296
                                32.814 24.564 21.160 1.00 13.82
                                                              PROT
     ATOM
     ATOM
            609 C LEU 296
                              30.415 23.783 17.493 1.00 31.88
                                                             PROT
            610 O LEU 296
                               29.890 22.890 16.827 1.00 45.99
                                                             PROT
50
     ATOM
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30.884 24.912 16.932 1.00 27.00
                                                            PROT
    ATOM
            611 N PRO 297
                               31.423 26.037 17.708 1.00 36.12
                                                             PROT
            612 CD PRO 297
    ATOM
                                                             PROT
                               30.856 25.222 15.492 1.00 22.30
            613 CA PRO 297
    ATOM
                               31.182 26.716 15.424 1.00 16.06
                                                             PROT
    ATOM
            614 CB PRO 297
                               31.107 27.208 16.827 1.00 42.41
    ATOM
           615 CG PRO 297
                                                             PROT
                              31.838 24.413 14.642 1.00 28.19
                                                            PROT
            616 C PRO 297
    ATOM
                              32.983 24.189 15.036 1.00 39.38
                                                            PROT
    ATOM 617 O PRO 297
                              31.371 24.014 13.457 1.00 35.37
    ATOM
           618 N CYS 298
                                                            PROT
                               32.134 23.233 12.481 1.00 32.41
                                                             PROT
           619 CA CYS 298
    ATOM
                              31.416 23.289 11.112 1.00 40.85
                                                             PROT
           620 CB CYS 298
10
    ATOM
                              32.431 23.615 9.614 1.00 61.24
           621 SG CYS 298
                                                            PROT
    ATOM
                              33.596 23.654 12.352 1.00 31.68
                                                            PROT
    ATOM 622 C CYS 298
           623 O CYS 298
                              34.474 22.804 12.225 1.00 28.49
                                                            PROT
    ATOM
                              33.869 24.954 12.393 1.00 29.93
                                                            PROT
            624 N GLU 299
    ATOM
                               35.253 25.407 12.278 1.00 36.38
                                                             PROT
           625 CA GLU 299
    ATOM
15
                               35.346 26.931 12.203 1.00 32.78
                                                             PROT
    ATOM 626 CB GLU 299
    ATOM 627 CG GLU 299
                               34.467 27.546 11.167 1.00 43.40
                                                             PROT
    ATOM 628 CD GLU 299
                               33.038 27.593 11.625 1.00 58.19
                                                             PROT
                                                             PROT
                               32,723 28,457 12,474 1.00 67,37
    ATOM 629 OE1 GLU 299
                                                              PROT
    ATOM 630 OE2 GLU 299
                               32.237 26.762 11.143 1.00 54.02
20
    ATOM 631 C GLU 299
                              36.057 24.932 13.475 1.00 38.89
                                                            PROT
                              37.129 24.342 13.316 1.00 48.67
                                                            PROT
    ATOM 632 O GLU 299
                              35.528 25.186 14.671 1.00 36.49
                                                            PROT
           633 N ASP 300
    ATOM
    ATOM
           634 CA ASP 300
                              36.201 24.805 15.906 1.00 29.96
                                                             PROT
                              35.455 25.391 17.111 1.00 5.33
                                                            PROT
           635 CB ASP 300
25
    ATOM
                              35.830 26.853 17.378 1.00 19.10
                                                             PROT
           636 CG ASP 300
    ATOM
                               36,491 27.473 16.518 1.00 27.28
                                                             PROT
    ATOM 637 OD1 ASP 300
                               35.470 27.396 18.444 1.00 23.55
            638 OD2 ASP 300
                                                             PROT
    ATOM
                              36.380 23.294 16.054 1.00 25.88
                                                            PROT
           639 C ASP 300
    ATOM
                              37.441 22.845 16.484 1.00 19.03
                                                            PROT
           640 O ASP 300
30
    ATOM
                              35.360 22.516 15.689 1.00 6.29
            641 N GLN 301
                                                            PROT
    ATOM
                                                             PROT
            642 CA GLN 301
                              35.432 21.055 15.769 1.00 9.51
    ATOM
                               34.170 20.421 15.183 1.00 18.27
                                                             PROT
            643 CB GLN 301
    ATOM
                               32.886 20.813 15.875 1.00 28.72
                                                             PROT
    ATOM
           644 CG GLN 301
                               31.676 20.155 15.243 1.00 17.63
                                                             PROT
    ATOM 645 CD GLN 301
35
                                                              PROT
    ATOM 646 OE1 GLN 301
                               31.689 19.823 14.060 1.00 30.65
           647 NE2 GLN 301
                               30.625 19.965 16.027 1.00 30.44
                                                              PROT
    ATOM
                              36.646 20.491 15.020 1.00 15.48
                                                            PROT
     ATOM 648 C GLN 301
                              37.333 19.584 15.500 1.00 21.96
                                                            PROT
           649 O GLN 301
     ATOM
                             36.891 21.014 13.825 1.00 24.00
            650 N ILE 302
                                                            PROT
40
     ATOM
     ATOM 651 CA ILE 302
                              38.011 20.555 13.026 1.00 28.84
                                                            PROT
           652 CB ILE 302
                              37.930 21.112 11.607 1.00 33.13
                                                            PROT
     ATOM
                              39.147 20.690 10.813 1.00 37.90
                                                             PROT
     ATOM
            653 CG2 ILE 302
                               36.656 20.610 10.941 1.00 29.63
     ATOM 654 CG1 ILE 302
                                                             PROT
                               36.296 21.356 9.698 1.00 32.99
                                                            PROT
           655 CD1 ILE 302
45
     ATOM
                             39.308 21.014 13.670 1.00 28.73
                                                            PROT
     ATOM
           656 C ILE 302
            657 O ILE 302
                             40.219 20.219 13.895 1.00 36.02
                                                            PROT
     ATOM
                             39.396 22.304 13.968 1.00 25.04
                                                            PROT
            658 N ILE 303
     ATOM
                             40.590 22.817 14.603 1.00 24.27
                                                            PROT
     ATOM
            659 CA ILE 303
                              40.414 24.270 15.054 1.00 20.89
                                                            PROT
            660 CB ILE 303
50
     ATOM
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41.686 24.740 15.744 1.00 32.38
                                                              PROT
     ATOM
            661 CG2 ILE 303
            662 CG1 ILE 303
                               40.079 25.158 13.849 1.00 18.88
                                                             PROT
     ATOM
            663 CD1 ILE 303
                               40.298 26.648 14.079 1.00 5.31
                                                             PROT
    ATOM
                              40.861 21.948 15.825 1.00 26.92
                                                            PROT
     ATOM
            664 C ILE 303
            665 O ILE 303
                              41.963 21.440 15.997 1.00 31.32
                                                            PROT
     ATOM
            666 N LEU 304
                              39.843 21.763 16.659 1.00 11.00
                                                             PROT
     ATOM
                               39.983 20.953 17.854 1.00 7.21
                                                             PROT
    ATOM
            667 CA LEU 304
                               38.663 20.886 18.613 1.00 2.00
                                                             PROT
            668 CB LEU 304
     ATOM
     ATOM
            669 CG LEU 304
                               38.633 21.511 20.012 1.00 8.04
                                                             PROT
                                39.383 22.812 19.997 1.00 2.00
                                                              PROT
     ATOM
            670 CD1 LEU 304
10
                                37.188 21.729 20.472 1.00 4.99
            671 CD2 LEU 304
                                                              PROT
     ATOM
                              40.441 19.554 17.507 1.00 4.64
            672 C LEU 304
                                                            PROT
     ATOM
     ATOM
            673 O LEU 304
                              41.368 19.032 18.119 1.00 14.88
                                                             PROT
                              39.807 18.953 16.510 1.00 4.55
            674 N LEU 305
                                                             PROT
     ATOM
                               40.140 17.590 16.093 1.00 7.03
     ATOM
            675 CA LEU 305
                                                             PROT
15
                               39.099 17.098 15.104 1.00 3.70
                                                             PROT
            676 CB LEU 305
     ATOM
            677 CG LEU 305
                               38.164 16.054 15.691 1.00 10.31
                                                              PROT
    ATOM
                                36.744 16.340 15.245 1.00 2.00
            678 CD1 LEU 305
                                                              PROT
     ATOM
            679 CD2 LEU 305
                                38.629 14.665 15.260 1.00 9.42
                                                              PROT
     ATOM
                              41.527 17.418 15.483 1.00 10.17
            680 C LEU 305
                                                             PROT
20
     ATOM
            681 O LEU 305
                              42.174 16.374 15.651 1.00 7.58
                                                             PROT
     ATOM
                              41.975 18.442 14.765 1.00 9.98
                                                            PROT
     ATOM
            682 N LYS 306
                               43,283 18,408 14,127 1.00 9.14
                                                             PROT
            683 CA LYS 306
     ATOM
                               43.409 19.558 13.131 1.00 18.85
                                                             PROT
            684 CB LYS 306
     ATOM
                                                              PROT
25
     ATOM
            685 CG LYS 306
                               42.815 19.270 11.763 1.00 25.44
            686 CD LYS 306
                               42.198 20.529 11.178 1.00 29.07
                                                              PROT
     ATOM
                               42.698 20.808 9.774 1.00 37.81
                                                             PROT
            687 CE LYS 306
     ATOM
            688 NZ LYS 306
                               43.867 19.964 9.403 1.00 30.48
                                                             PROT
     ATOM
     ATOM
            689 C LYS 306
                              44.376 18.522 15.175 1.00 7.31
                                                            PROT
                              45.439 17.919 15.048 1.00 16.95
                                                             PROT
30
     ATOM
            690 O LYS 306
            691 N GLY 307
                               44.097 19.295 16.218 1.00 12.67
                                                             PROT
     ATOM
            692 CA GLY 307
                               45.062 19.484 17.279 1.00 7.25
                                                             PROT
     ATOM
     ATOM
            693 C GLY 307
                               45.297 18.269 18.150 1.00 15.08
                                                             PROT
            694 O GLY 307
                               46.441 17.972 18.488 1.00 20.11
                                                             PROT
     ATOM
            695 N CYS 308
                               44.225 17.552 18.481 1.00 8.29
                                                             PROT
     ATOM
35
                               44.286 16.380 19.364 1.00 3.44
                                                             PROT
            696 CA CYS 308
     ATOM
                               43.097 16.402 20.326 1.00 14.26
                                                              PROT
            697 CB CYS 308
     ATOM
                                                             PROT
            698 SG CYS 308
                               41.539 15.750 19.634 1.00 21.83
     ATOM
            699 C CYS 308
                              44.344 14.995 18.738 1.00 8.37
                                                             PROT
     ATOM
                               44.502 13.997 19.453 1.00 10.98
                                                             PROT
            700 O CYS 308
40
     ATOM
                               44.202 14.916 17.420 1.00 10.83
            701 N CYS 309
                                                             PROT
     ATOM
            702 CA CYS 309
                               44.236 13.625 16.752 1.00 3.22
                                                             PROT
     ATOM
            703 CB CYS 309
                               44.240 13.831 15.240 1.00 15.79
                                                              PROT
     ATOM
                               43.683 12.402 14.319 1.00 25.54
                                                              PROT
     ATOM
            704 SG CYS 309
            705 C CYS 309
                              45.439 12.767 17.193 1.00 2.00
                                                             PROT
45
     ATOM
                               45.251 11.722 17.807 1.00 12.28
                                                             PROT
            706 O CYS 309
     ATOM
                               46.663 13.205 16.900 1.00 2.00
                                                             PROT
     ATOM
            707 N MET 310
            708 CA MET 310
                               47.858 12.446 17.286 1.00 2.00
                                                             PROT
     ATOM
                                49.122 13.171 16.860 1.00 2.00
                                                              PROT
            709 CB MET 310
     ATOM
                                49.975 12.422 15.880 1.00 5.92
                                                              PROT
50
     ATOM
            710 CG MET 310
```

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50.481 10.805 16.368 1.00 22.47
                                                              PROT
    ATOM
            711 SD MET 310
            712 CE MET 310
                               52.140 11.112 16.808 1.00 20.84
                                                              PROT
    ATOM
                              47.941 12.239 18.793 1.00 11.95
                                                             PROT
    ATOM
            713 C MET 310
                              48.455 11.220 19.270 1.00 15.53
                                                             PROT
    ATOM
            714 O MET 310
    ATOM
            715 N GLU 311
                              47.463 13.225 19.542 1.00 6.79
                                                            PROT
 5
                               47.493 13.139 20.979 1.00 2.00
                                                             PROT
            716 CA GLU 311
    ATOM
                               46.932 14.427 21.581 1.00 6.42
                                                             PROT
            717 CB GLU 311
    ATOM
    ATOM
            718 CG GLU 311
                               47.880 15.619 21.436 1.00 8.40
                                                             PROT
                               47.236 16.940 21.820 1.00 14.10
                                                              PROT
            719 CD GLU 311
    ATOM
                               46.157 16.895 22.434 1.00 16.54
                                                              PROT
            720 OE1 GLU 311
10
    ATOM
                               47.795 18.020 21.515 1.00 4.09
    ATOM
            721 OE2 GLU 311
                                                             PROT
                              46.683 11.923 21.406 1.00 7.80
    ATOM
            722 C GLU 311
                                                            PROT
                              47.195 11.026 22.067 1.00 14.07
                                                             PROT
            723 O GLU 311
    ATOM
                             45.425 11.873 21.001 1.00 2.00
                                                           PROT
    ATOM
            724 N ILE 312
                              44.574 10.752 21.371 1.00 3.60
                                                            PROT
            725 CA ILE 312
15
    ATOM
                              43,114 11.013 20.947 1.00 2.00
            726 CB ILE 312
                                                            PROT
    ATOM
                               42.277 9.769 21.145 1.00 2.00
                                                            PROT
    ATOM
            727 CG2 ILE 312
            728 CG1 ILE 312
                               42.579 12.221 21.727 1.00 2.00
                                                            PROT
    ATOM
            729 CD1 ILE 312
                               41.118 12.555 21.495 1.00 2.00
                                                            PROT
    ATOM
            730 C ILE 312
                             45.049 9.437 20.760 1.00 8.32
                                                           PROT
20
     ATOM
    ATOM
            731 O ILE 312
                             44.918 8.373 21.370 1.00 5.58
                                                           PROT
            732 N MET 313
                               45.615 9.501 19.563 1.00 3.98
                                                            PROT
    ATOM
                               46.054 8.282 18.905 1.00 8.91
                                                             PROT
     ATOM
            733 CA MET 313
     ATOM
            734 CB MET 313
                               46.455 8.572 17.462 1.00 25.71
                                                             PROT
            735 CG MET 313
                               45.430 8.111 16.431 1.00 22.86
                                                             PROT
    ATOM
25
                               45.955 8.430 14.736 1.00 20.60
                                                             PROT
            736 SD MET 313
    ATOM
                               45,412 10.055 14.534 1.00 14.95
                                                             PROT
     ATOM
            737 CE MET 313
            738 C MET 313
                              47.211 7.634 19.635 1.00 12.95
                                                            PROT
     ATOM
                               47.213 6.426 19.857 1.00 22.09
                                                            PROT
            739 O MET 313
     ATOM
                              48.190 8.442 20.021 1.00 10.79
                                                            PROT
            740 N SER 314
30
     ATOM
                               49.354 7.935 20.719 1.00 2.00
                                                            PROT
            741 CA SER 314
     ATOM
                                                            PROT
            742 CB SER 314
                               50.399 9.042 20.816 1.00 7.24
    ATOM
                               50.453 9.815 19.619 1.00 10.89
                                                            PROT
            743 OG SER 314
     ATOM
                              48.991 7.399 22.105 1.00 8.64
                                                           PROT
     ATOM
            744 C SER 314
                              49.559 6.392 22.558 1.00 5.72
                                                            PROT
35
     A·TOM
            745 O SER 314
            746 N LEU 315
                                                            PROT
                              48.050 8.062 22.782 1.00 2.00
     ATOM
                               47.628 7.605 24.104 1.00 2.00
                                                            PROT
     ATOM
            747 CA LEU 315
     ATOM
                               46.521 8.502 24.671 1.00 2.95
                                                            PROT
            748 CB LEU 315
                               45.831 8.096 25.992 1.00 2.00
                                                            PROT
            749 CG LEU 315
     ATOM
            750 CD1 LEU 315
                                46.876 7.845 27.072 1.00 2.54
                                                             PROT
40
     ATOM
            751 CD2 LEU 315
                                44.865 9.182 26.444 1.00 2.00
                                                             PROT
     ATOM
                                                            PROT
                              47.107 6.182 23.945 1.00 3.25
     ATOM
            752 C LEU 315
                                                            PROT
     ATOM
            753 O LEU 315
                              47.568 5.253 24.603 1.00 2.00
            754 N ARG 316
                               46.157 6.010 23.039 1.00 7.28
                                                            PROT
     ATOM
                               45.588 4.691 22.808 1.00 13.31
            755 CA ARG 316
                                                             PROT
45
     ATOM
                               44.551 4.758 21.693 1.00 11.11
                                                             PROT
     ATOM
            756 CB ARG 316
                               43.545 5.872 21.887 1.00 10.55
                                                             PROT
     ATOM
            757 CG ARG 316
                               42.354 5.639 21.012 1.00 10.09
                                                             PROT
            758 CD ARG 316
     ATOM
                               41.131 6.149 21.605 1.00 12.29
                                                             PROT
     ATOM
            759 NE ARG 316
                               39.955 6.127 20.994 1.00 6.99
                                                             PROT
            760 CZ ARG 316
50
     ATOM
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38.880 6.608 21.595 1.00 19.32
                                                               PROT
     ATOM
            761 NH1 ARG 316
            762 NH2 ARG 316
                                39.853 5.619 19.778 1.00 17.16
                                                               PROT
     ATOM
                               46.666 3.686 22.458 1.00 10.10
                                                             PROT
     ATOM
            763 C ARG 316
                               46.549 2.508 22.753 1.00 14.94
                                                             PROT
     ATOM
            764 O ARG 316
     ATOM
            765 N ALA 317
                               47.723 4.148 21.819 1.00 6.51
                                                             PROT
 5
                                48.801 3.243 21.474 1.00 11.04
                                                             PROT
     ATOM
            766 CA ALA 317
                                                              PROT
            767 CB ALA 317
                               49.749 3.902 20.487 1.00 16.13
     ATOM
     ATOM
            768 C ALA 317
                               49.539 2.910 22.753 1.00 12.70
                                                             PROT
                               49.822 1.755 23.033 1.00 23.09
            769 O ALA 317
                                                             PROT
     ATOM
            770 N ALA 318
                               49.832 3.943 23.534 1.00 14.79
                                                             PROT
     ATOM
10
     ATOM
            771 CA ALA 318
                                50.567 3.779 24.776 1.00 8.38
                                                             PROT
     ATOM
            772 CB ALA 318
                                50.727 5.122 25.448 1.00 11.75
                                                              PROT
            773 C ALA 318
                               49.941 2.786 25.741 1.00 10.30
                                                             PROT
     ATOM
     ATOM
            774 O ALA 318
                               50.585 1.824 26.165 1.00 8.48
                                                             PROT
     ATOM
            775 N VAL 319
                               48.680 3.011 26.083 1.00 7.87
                                                             PROT
15
            776 CA VAL 319
                                48.002 2.131 27.027 1.00 9.64
                                                             PROT
     ATOM
                                46.579 2.622 27.334 1.00 2.57
                                                             PROT
     ATOM
            777 CB VAL 319
            778 CG1 VAL 319
                                46.644 3.929 28.127 1.00 5.09
                                                              PROT
     ATOM
            779 CG2 VAL 319
                                45.807 2.823 26.043 1.00 5.15
                                                              PROT
     ATOM
                               47.930 0.695 26.541 1.00 11.68
            780 C VAL 319
                                                             PROT
20
     ATOM
     ATOM
            781 O VAL 319
                               47.440 -0.171 27.254 1.00 16.32
                                                             PROT
            782 N ARG 320
                               48.415 0.444 25.329 1.00 16.40
                                                             PROT
     ATOM
                                48.405 -0.902 24.767 1.00 13.20
            783 CA ARG 320
                                                              PROT
     ATOM
     ATOM
            784 CB ARG 320
                                47.736 -0.918 23.393 1.00 2.00
                                                              PROT
                                46.310 -0.405 23.420 1.00 14.07
25
     ATOM
            785 CG ARG 320
                                                              PROT
                                45.283 -1.460 23.035 1.00 19.69
                                                              PROT
     ATOM
            786 CD ARG 320
                                44.168 -0.868 22.292 1.00 36.52
                                                              PROT
     ATOM
            787 NE ARG 320
     ATOM
            788 CZ ARG 320
                                42.912 -1.313 22.322 1.00 47.43
                                                              PROT
                                41.966 -0.705 21.609 1.00 43.57
                                                              PROT
     ATOM
            789 NH1 ARG 320
                                                               PROT
            790 NH2 ARG 320
                                42.596 -2.367 23.061 1.00 49.93
30
     ATOM
            791 C ARG 320
                               49.835 -1.391 24.662 1.00 15.45
                                                             PROT
     ATOM
            792 O ARG 320
                               50.167 -2.218 23.809 1.00 24.78
                                                             PROT
     ATOM
            793 N TYR 321
                               50.684 -0.860 25.537 1.00 13.68
                                                             PROT
     ATOM
     ATOM
            794 CA TYR 321
                                52.085 -1.258 25.572 1.00 18.80
                                                              PROT
                                52.925 -0.208 26.295 1.00 9.64
                                                             PROT
35
     ATOM
            795 CB TYR 321
                                54.313 -0.685 26.622 1.00 11.20
            796 CG TYR 321
                                                              PROT
     ATOM
                                55.211 -1.005 25.612 1.00 2.00
                                                              PROT
     ATOM
            797 CD1 TYR 321
     ATOM
            798 CE1 TYR 321
                                56.483 -1.461 25.906 1.00 9.63
                                                              PROT
            799 CD2 TYR 321
                                54.727 -0.834 27.943 1.00 18.93
                                                              PROT
     ATOM
                                56.003 -1.293 28.250 1.00 19.49
                                                              PROT
40
     ATOM
            800 CE2 TYR 321
                                56.874 -1.604 27.225 1.00 14.75
                                                              PROT
     ATOM
            801 CZ TYR 321
            802 OH TYR 321
                                58.137 -2.053 27.518 1.00 22.96
                                                              PROT
     ATOM
     ATOM
            803 C TYR 321
                               52.209 -2.607 26.287 1.00 19.74
                                                             PROT
     ATOM
            804 O TYR 321
                               51.483 -2.889 27.242 1.00 31.56
                                                             PROT
            805 N ASP 322
                               53.136 -3.435 25.823 1.00 26.35
                                                             PROT
45
     ATOM
     ATOM
            806 CA ASP 322
                               53.346 -4.759 26.392 1.00 22.38
                                                              PROT
                               52.982 -5.814 25.353 1.00 33.63
     ATOM
            807 CB ASP 322
                                                              PROT
            808 CG ASP 322
                               52.601 -7.128 25.970 1.00 40.70
                                                              PROT
     ATOM
     ATOM
            809 OD1 ASP 322
                               51.539 -7.658 25.591 1.00 48.18
                                                              PROT
                                53.358 -7.628 26.826 1.00 38.91
50
            810 OD2 ASP 322
                                                              PROT
     ATOM
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	ATOM	811 C ASP 322	54.800 -4.928 26.776 1.00 23.51	PROT
	ATOM	812 O ASP 322	55.683 -4.844 25.924 1.00 37.80	PROT
	ATOM	812 O ASI 322 813 N PRO 323	55.076 -5.160 28.066 1.00 24.06	PROT
	ATOM	814 CD PRO 323	54.130 -5.258 29.187 1.00 19.35	PROT
5	ATOM	814 CD TRO 323 815 CA PRO 323	56.462 -5.339 28.507 1.00 23.60	PROT
J	ATOM	816 CB PRO 323	56.390 -5.121 30.007 1.00 3.90	PROT
	ATOM	817 CG PRO 323	55.031 -5.570 30.360 1.00 14.06	PROT
	ATOM	817 CG TRO 323 818 C PRO 323	56.949 -6.736 28.151 1.00 21.79	PROT
	ATOM	819 O PRO 323	58.149 -7.003 28.119 1.00 27.28	PROT
10	ATOM	820 N GLU 324	56.009 -7.633 27.889 1.00 37.63	PROT
10	ATOM	820 N GLU 324 821 CA GLU 324	56.366 -8.993 27.524 1.00 37.63	PROT
		821 CA GLO 324 822 CB GLU 324	55.133 -9.885 27.551 1.00 37.58	PROT
	ATOM		56.971 -8.956 26.124 1.00 43.28	PROT
	ATOM	823 C GLU 324	58.154 -9.239 25.938 1.00 43.14	PROT
15	ATOM	824 O GLU 324	56.153 -8.586 25.142 1.00 31.72	
15	ATOM	825 N SER 325	56.607 -8.508 23.765 1.00 30.34	PROT
	ATOM	826 CA SER 325		PROT
	ATOM	827 CB SER 325	55.413 -8.522 22.814 1.00 17.63	PROT
	ATOM	828 OG SER 325	54.356 -7.729 23.315 1.00 31.90	PROT
20	ATOM	829 C SER 325	57.441 -7.257 23.519 1.00 31.94	PROT
20	ATOM	830 O SER 325	58.146 -7.169 22.513 1.00 45.47	PROT
	ATOM	831 N GLU 326	57.359 -6.289 24.429 1.00 31.10	PROT
	ATOM	832 CA GLU 326	58.119 -5.050 24.281 1.00 31.43	PROT
	ATOM	833 CB GLU 326	59.598 -5.382 24.091 1.00 30.39	PROT
25	ATOM	834 CG GLU 326	60.552 -4.342 24.612 1.00 35.00	PROT
25	ATOM	835 CD GLU 326	61.738 -4.965 25.304 1.00 29.12	PROT
	ATOM	836 OE1 GLU 326	61.525 -5.579 26.370 1.00 39.21	PROT
	ATOM	837 OE2 GLU 326	62.872 -4.844 24.788 1.00 29.11	PROT
	ATOM	838 C GLU 326	57.605 -4.283 23.063 1.00 28.37	PROT
20	ATOM	839 O GLU 326	58.382 -3.677 22.321 1.00 26.51	PROT
30	ATOM	840 N THR 327	56.290 -4.301 22.873 1.00 23.71	PROT
	ATOM	841 CA THR 327	55.674 -3.648 21.720 1.00 22.11	PROT
	ATOM	842 CB THR 327	55.298 -4.705 20.652 1.00 28.08	PROT
	ATOM	843 OG1 THR 327	54.226 -5.524 21.145 1.00 16.87	PROT
2.5	ATOM	844 CG2 THR 327	56.494 -5.597 20.340 1.00 24.03	PROT
35	ATOM	845 C THR 327	54.420 -2.824 22.046 1.00 22.42	PROT
	ATOM	846 O THR 327	53.928 -2.830 23.172 1.00 17.50	PROT
	ATOM	847 N LEU 328	53.914 -2.122 21.038 1.00 17.28	PROT
	ATOM	848 CA LEU 328	52.728 -1.285 21.171 1.00 14.83	PROT
4.0	ATOM	849 CB LEU 328	53.065 0.157 20.806 1.00 15.27	PROT
40	ATOM	850 CG LEU 328	53.693 1.036 21.879 1.00 10.50	PROT
	ATOM	851 CD1 LEU 328	54.137 2.336 21.254 1.00 16.75	PROT
	ATOM	852 CD2 LEU 328	52.682 1.285 22.979 1.00 20.19	PROT
	ATOM	853 C LEU 328	51.687 -1.804 20.198 1.00 18.16	PROT
	ATOM	854 O LEU 328	52.035 -2.508 19.254 1.00 23.88	PROT
45	ATOM	855 N THR 329	50.421 -1.450 20.402 1.00 9.40	PROT
	ATOM	856 CA THR 329	49.389 -1.920 19.495 1.00 8.26	PROT
	ATOM	857 CB THR 329	48.460 -2.888 20.199 1.00 8.67	PROT
	ATOM	858 OG1 THR 329	49.213 -4.052 20.577 1.00 13.23	PROT
	ATOM	859 CG2 THR 329	47.308 -3.289 19.270 1.00 2.00	PROT
50	ATOM	860 C THR 329	48.569 -0.841 18.800 1.00 16.65	PROT

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47.726 -0.158 19.406 1.00 17.20
                                                            PROT
     ATOM
            861 O THR 329
     ATOM
            862 N LEU 330
                              48.808 -0.725 17.495 1.00 21.56
                                                            PROT
    ATOM
            863 CA LEU 330
                               48.138 0.258 16.655 1.00 20.95
                                                             PROT
                               49.106 0.676 15.539 1.00 17.36
                                                             PROT
            864 CB LEU 330
    ATOM
                               50.570 0.797 16.028 1.00 12.86
            865 CG LEU 330
                                                             PROT
    ATOM
5
                               51.531 0.521 14.898 1.00 10.10
            866 CD1 LEU 330
    ATOM
                                                             PROT
            867 CD2 LEU 330
                               50.830 2.180 16.600 1.00 2.00
                                                             PROT
    ATOM
                              46.803 -0.258 16.097 1.00 21.35
    ATOM 868 C LEU 330
                                                            PROT
    ATOM
           869 O LEU 330
                              46.655 -1.444 15.791 1.00 21.93
                                                            PROT
            870 N ASN 331
                              45.834 0.648 15.987 1.00 27.76
                                                            PROT
10
    ATOM
            871 CA ASN 331
                               44.487 0.338 15.498 1.00 28.09
                                                             PROT
    ATOM
                               44.460 0.275 13.971 1.00 24.95
                                                             PROT
    ATOM
           872 CB ASN 331
                               43.074 0.540 13.397 1.00 33.45
                                                             PROT
    ATOM 873 CG ASN 331
            874 OD1 ASN 331
                                42.512 -0.305 12.701 1.00 38.21
                                                              PROT
    ATOM
                                42.522 1.715 13.680 1.00 24.73
            875 ND2 ASN 331
                                                             PROT
15
    ATOM
            876 C ASN 331
                              43.946 -0.967 16.075 1.00 32.03
                                                            PROT
    ATOM
            877 O ASN 331
                              43.166 -1.668 15.431 1.00 35.49
                                                            PROT
    ATOM
            878 N GLY 332
                              44.357 -1.282 17.299 1.00 40.24
                                                            PROT
     ATOM
    ATOM
            879 CA GLY 332
                               43.894 -2.495 17.941 1.00 38.04
                                                             PROT
            880 C GLY 332
                              44.009 -3.665 16.998 1.00 40.09
                                                            PROT
20
    ATOM
            881 O GLY 332
                              43.001 -4.225 16.563 1.00 45.79
                                                            PROT
    ATOM
            882 N GLU 333
                              45.249 -4.013 16.664 1.00 41.60
                                                            PROT
    ATOM
            883 CA GLU 333
                               45.539 -5.126 15.763 1.00 36.28
                                                             PROT
    ATOM
                               44.752 -4.978 14.454 1.00 46.39
                                                             PROT
            884 CB GLU 333
    ATOM
    ATOM 885 CG GLU 333
                               44.745 -3.580 13.862 1.00 58.03
                                                             PROT
25
                               43.883 -3.485 12.610 1.00 67.00
    ATOM 886 CD GLU 333
                                                             PROT
                                                              PROT
            887 OE1 GLU 333
                               44.446 -3.282 11.511 1.00 67.51
    ATOM
                                42.644 -3.615 12.727 1.00 71.01
            888 OE2 GLU 333
                                                              PROT
     ATOM
    ATOM
            889 C GLU 333
                              47.027 -5.266 15.446 1.00 33.13
                                                            PROT
                              47.563 -6.366 15.486 1.00 27.97
                                                            PROT
    ATOM
            890 O GLU 333
30
                                                             PROT
            891 N MET 334
                              47.692 -4.152 15.143 1.00 27.00
    ATOM
                                                             PROT
    ATOM
           892 CA MET 334
                               49.111 -4.188 14.798 1.00 29.83
                               49.416 -3.159 13.699 1.00 26.04
                                                             PROT
    ATOM
            893 CB MET 334
            894 CG MET 334
                               50.561 -3.588 12.765 1.00 28.06
                                                             PROT
    ATOM
           895 SD MET 334
                               51.263 -2.273 11.736 1.00 28.46
                                                             PROT
35
    ATOM
                               50.021 -2.123 10.497 1.00 22.48
                                                             PROT
    ATOM
            896 CE MET 334
                               50.087 -3.995 15.959 1.00 33.52
                                                            PROT
     ATOM
            897 C MET 334
                               50.071 -2.962 16.631 1.00 35.81
                                                             PROT
    ATOM
            898 O MET 334
    ATOM
            899 N ALA 335
                              50.942 -4.996 16.171 1.00 27.46
                                                            PROT
            900 CA ALA 335
                               51.948 -4.976 17.234 1.00 29.69
                                                             PROT
     ATOM
40
     ATOM
            901 CB ALA 335
                               51.966 -6.314 17.965 1.00 12.67
                                                             PROT
     ATOM
            902 C ALA 335
                              53.336 -4.682 16.662 1.00 31.74
                                                            PROT
            903 O ALA 335
                              53.943 -5.530 16.009 1.00 43.66
                                                            PROT
    ATOM
            904 N VAL 336
                              53.848 -3.489 16.923 1.00 23.98
                                                            PROT
    ATOM
45
    ATOM
            905 CA VAL 336
                               55.151 -3.118 16.405 1.00 21.32
                                                             PROT
            906 CB VAL 336
                               55.028 -1.873 15.504 1.00 17.37
                                                             PROT
     ATOM
                                                             PROT
            907 CG1 VAL 336
                               53,945 -2.104 14.462 1.00 14.88
     ATOM
     ATOM
            908 CG2 VAL 336
                                54.686 -0.648 16.339 1.00 15.53
                                                             PROT
                              56.150 -2.852 17.526 1.00 22.72
                                                            PROT
            909 C VAL 336
    ATOM
                                                            PROT
50
    ATOM
            910 O VAL 336
                              55.763 -2.540 18.651 1.00 25.15
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	ATOM	911 N THR 337	57.435 -3.001 17.220 1.00 19.21	PROT
	ATOM	912 CA THR 337	58.476 -2.765 18.205 1.00 20.31	PROT
	ATOM	913 CB THR 337	59.752 -3.578 17.884 1.00 14.76	PROT
	ATOM	914 OG1 THR 337	59.957 -3.616 16.467 1.00 16.43	PROT
5	ATOM	915 CG2 THR 337	59.615 -4.995 18.393 1.00 7.08	PROT
	ATOM	916 C THR 337	58.785 -1.272 18.157 1.00 24.20	PROT
	ATOM	917 O THR 337	58.322 -0.591 17.245 1.00 28.05	PROT
	ATOM	918 N ARG 338	59.548 -0.766 19.134 1.00 27.55	PROT
	ATOM	919 CA ARG 338	59.917 0.655 19.197 1.00 16.80	PROT
10	ATOM	920 CB ARG 338	60.757 0.942 20.446 1.00 17.04	PROT
	ATOM	921 CG ARG 338	61.687 2.149 20.303 1.00 9.79	PROT
	ATOM	922 CD ARG 338	62.666 2.276 21.458 1.00 2.00	PROT
	ATOM	923 NE ARG 338	61.994 2.128 22.739 1.00 20.70	PROT
	ATOM	924 CZ ARG 338	61.897 3.083 23.657 1.00 12.04	PROT
15	ATOM	925 NH1 ARG 338	61.261 2.840 24.784 1.00 27.11	PROT
13	ATOM	926 NH2 ARG 338	62.436 4.272 23.459 1.00 22.23	PROT
	ATOM	927 C ARG 338	60.702 1.085 17.968 1.00 21.26	PROT
	ATOM	927 C ARG 338 928 O ARG 338	60.338 2.049 17.295 1.00 16.40	PROT
	ATOM	929 N GLY 339	61.792 0.374 17.693 1.00 31.57	PROT
20	ATOM	930 CA GLY 339	62.609 0.696 16.540 1.00 32.42	PROT
20	ATOM	930 CA GL1 337 931 C GLY 339	61.816 0.534 15.254 1.00 30.08	PROT
		931 C GL1 339 932 O GLY 339	61.932 1.342 14.328 1.00 25.82	PROT
	ATOM		61.008 -0.520 15.192 1.00 16.60	PROT
	ATOM		60.191 -0.768 14.012 1.00 14.08	PROT
25	ATOM		59.199 -1.884 14.301 1.00 5.73	PROT
25	ATOM		58.849 -2.697 13.100 1.00 16.15	PROT
	ATOM	936 CG GLN 340		
	ATOM	937 CD GLN 340	58.577 -4.141 13.442 1.00 22.46	PROT
	ATOM	938 OE1 GLN 340	57.767 -4.450 14.316 1.00 30.45	PROT
• •	ATOM	939 NE2 GLN 340	59.254 -5.040 12.749 1.00 34.19	PROT
30	ATOM	940 C GLN 340	59.452 0.521 13.632 1.00 22.07	PROT
	ATOM	941 O GLN 340	59.707 1.103 12.576 1.00 21.13	PROT
	ATOM	942 N LEU 341	58.561 0.976 14.518 1.00 27.88	PROT
	ATOM	943 CA LEU 341	57.778 2.197 14.306 1.00 21.82	PROT
	ATOM	944 CB LEU 341	56.813 2.418 15.483 1.00 10.20	PROT
35	ATOM	945 CG LEU 341	55.930 3.682 15.534 1.00 16.27	PROT
	ATOM	946 CD1 LEU 341	54.777 3.618 14.518 1.00 13.27	PROT
	ATOM	947 CD2 LEU 341	55.370 3.822 16.935 1.00 10.68	PROT
	ATOM	948 C LEU 341	58.683 3.413 14.138 1.00 13.98	PROT
	ATOM	949 O LEU 341	58.315 4.386 13.486 1.00 7.94	PROT
40	ATOM	950 N LYS 342	59.867 3.361 14.734 1.00 11.48	PROT
	ATOM	951 CA LYS 342	60.804 4.465 14.613 1.00 17.77	PROT
	ATOM	952 CB LYS 342	62.063 4.213 15.459 1.00 13.58	PROT
	ATOM	953 CG LYS 342	63.219 5.173 15.140 1.00 13.27	PROT
	ATOM	954 CD LYS 342	64.173 5.358 16.319 1.00 5.44	PROT
45	ATOM	955 CE LYS 342	64.500 6.829 16.546 1.00 5.47	PROT
	ATOM	956 NZ LYS 342	65.721 7.019 17.388 1.00 4.98	PROT
	ATOM	957 C LYS 342	61.184 4.579 13.141 1.00 19.97	PROT
	ATOM	958 O LYS 342	60.939 5.595 12.501 1.00 20.34	PROT
	ATOM	959 N ASN 343	61.764 3.510 12.605 1.00 26.88	PROT
50	ATOM	960 CA ASN 343	62.196 3.470 11.219 1.00 22.34	PROT

```
62.829 2.123 10.929 1.00 4.80
            961 CB ASN 343
                                                           PROT
    ATOM
                                                           PROT
            962 CG ASN 343
                              64.060 1.894 11.758 1.00 18.77
    ATOM
            963 OD1 ASN 343
                               64.755 2.848 12.117 1.00 14.12
                                                            PROT
    ATOM
                               64.340 0.634 12.083 1.00 12.72
                                                            PROT
    ATOM
            964 ND2 ASN 343
            965 C ASN 343
                             61.091 3.736 10.224 1.00 20.40
                                                           PROT
    ATOM
    ATOM
            966 O ASN 343
                             61.309 4.417 9.232 1.00 20.76
                                                          PROT
                             59.908 3.200 10.494 1.00 12.62
                                                           PROT
    ATOM
            967 N GLY 344
            968 CA GLY 344
                              58.775 3.382 9.603 1.00 6.27
                                                           PROT
    ATOM
    ATOM
            969 C GLY 344
                             58.229 4.796 9.451 1.00 14.56
                                                          PROT
    ATOM
            970 O GLY 344
                             57.177 4.972 8.826 1.00 13.30
                                                          PROT
10
            971 N GLY 345
                             58.902 5.795 10.030 1.00 16.51
                                                           PROT
    ATOM
            972 CA GLY 345
                             58.439 7.166 9.869 1.00 20.04
                                                           PROT
    ATOM
                             58.248 8.112 11.046 1.00 25.64
    ATOM
            973 C GLY 345
                                                           PROT
           974 O GLY 345
                              58.243 9.331 10.849 1.00 23.32
                                                           PROT
    ATOM
                             58.099 7.588 12.260 1.00 22.22
    ATOM
            975 N LEU 346
                                                           PROT
15
                              57.874 8.449 13.415 1.00 14.94
                                                           PROT
            976 CA LEU 346
    ATOM
            977 CB LEU 346
                              57.070 7.700 14.474 1.00 3.92
                                                           PROT
    ATOM
                              55.566 7.538 14.193 1.00 5.92
                                                           PROT
    ATOM
            978 CG LEU 346
            979 CD1 LEU 346
                               54.938 6.796 15.355 1.00 2.00
                                                           PROT
    ATOM
            980 CD2 LEU 346
                               54.884 8.885 13.973 1.00 2.00
                                                           PROT
20
    ATOM
            981 C LEU 346
                             59.126 9.042 14.041 1.00 14.60
                                                           PROT
    ATOM
            982 O LEU 346
                             59.102 10.153 14.554 1.00 17.36
                                                           PROT
    ATOM
                             60.226 8.312 14.001 1.00 12.09
                                                           PROT
    ATOM
            983 N GLY 347
                             61.455 8.828 14.581 1.00 15.62
                                                          PROT
    ATOM
            984 CA GLY 347
25
    ATOM
            985 C GLY 347
                             61.439 8.963 16.090 1.00 6.31
                                                          PROT
                             60.865 8.141 16.790 1.00 13.15
                                                           PROT
    ATOM
           986 O GLY 347
                             62.076 10.011 16.592 1.00 13.74
                                                           PROT
    ATOM
            987 N VAL 348
            988 CA VAL 348
                             62.141 10.259 18.030 1.00 10.13
                                                            PROT
    ATOM
            989 CB VAL 348
                              62.757 11.646 18.342 1.00 9.26
                                                            PROT
    ATOM
                               61.867 12.752 17.794 1.00 2.00
                                                            PROT
    ATOM
            990 CG1 VAL 348
30
                               62.942 11.802 19.836 1.00 2.00
                                                            PROT
            991 CG2 VAL 348
    ATOM
           992 C VAL 348
                             60.763 10.216 18.650 1.00 6.61
                                                           PROT
    ATOM
            993 O VAL 348
                              60.619 10.066 19.862 1.00 3.12
                                                           PROT
    ATOM
            994 N VAL 349
                              59.746 10.358 17.816 1.00 5.51
                                                           PROT
    ATOM
                              58.386 10.342 18.306 1.00 2.00
            995 CA VAL 349
                                                            PROT
    ATOM
35
                              57.421 10.886 17.260 1.00 4.46
                                                            PROT
    ATOM
            996 CB VAL 349
            997 CG1 VAL 349
                               56.001 10.578 17.656 1.00 2.00
                                                            PROT
    ATOM
                               57.623 12.387 17.122 1.00 2.00
                                                           PROT
            998 CG2 VAL 349
    ATOM
                              57.995 8.933 18.687 1.00 9.15
    ATOM 999 C VAL 349
                                                          PROT
40
    ATOM 1000 O VAL 349
                              57.284 8.726 19.664 1.00 15.02
                                                           PROT
                              58.446 7.943 17.933 1.00 7.42
                                                           PROT
    ATOM 1001 N SER 350
    ATOM 1002 CA SER 350
                              58.087 6.590 18.315 1.00 12.87
                                                           PROT
                              58.695 5.561 17.382 1.00 9.48
                                                           PROT
    ATOM 1003 CB SER 350
    ATOM 1004 OG SER 350
                               58.529 4.269 17.931 1.00 10.82
                                                            PROT
    ATOM 1005 C SER 350
                              58.628 6.364 19.717 1.00 15.55
                                                           PROT
45
                              57.963 5.761 20.558 1.00 25.88
                                                           PROT
    ATOM 1006 O SER 350
    ATOM 1007 N ASP 351
                              59.838 6.863 19.950 1.00 16.38
                                                           PROT
                             60.522 6.743 21.230 1.00 9.58
                                                           PROT
    ATOM 1008 CA ASP 351
                              61.861 7.469 21.176 1.00 7.32
                                                           PROT
    ATOM 1009 CB ASP 351
50
    ATOM 1010 CG ASP 351
                               62.989 6.576 20.742 1.00 24.16
                                                            PROT
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ATOM 1011 OD1 ASP 351 64.011 7.110 20.275 1.00 30.24
                                                            PROT
    ATOM 1012 OD2 ASP 351
                               62.866 5.343 20.869 1.00 33.85
                                                          PROT
                             59.695 7.360 22.334 1.00 17.01
    ATOM 1013 C ASP 351
                                                          PROT
                              59.605 6.822 23.435 1.00 26.28
                                                           PROT
    ATOM 1014 O ASP 351
                              59.100 8.508 22.032 1.00 13.51
                                                           PROT
    ATOM 1015 N ALA 352
    ATOM 1016 CA ALA 352
                             58.294 9.224 23.004 1.00 5.19
                                                           PROT
                             57.914 10.593 22.452 1.00 2.00
                                                          PROT
    ATOM 1017 CB ALA 352
                              57.055 8.432 23.374 1.00 2.00
    ATOM 1018 C ALA 352
                                                          PROT
    ATOM 1019 O ALA 352
                              56.701 8.360 24.535 1.00 7.20
                                                          PROT
    ATOM 1020 N ILE 353
                             56.396 7.832 22.393 1.00 2.00
                                                          PROT
10
    ATOM 1021 CA ILE 353
                            55.201 7.049 22.677 1.00 5.90
                                                          PROT
                              54.468 6.626 21.381 1.00 5.87
                                                          PROT
    ATOM 1022 CB ILE 353
                            53.113 6.049 21.732 1.00 2.00
                                                          PROT
    ATOM 1023 CG2 ILE 353
    ATOM 1024 CG1 ILE 353
                              54.349 7.831 20.428 1.00 3.91
                                                           PROT
    ATOM 1025 CD1 ILE 353
                              53.330 7.664 19.294 1.00 2.00
                                                           PROT
15
    ATOM 1026 C ILE 353
                             55.554 5.795 23.484 1.00 12.46
                                                          PROT
    ATOM 1027 O ILE 353
                             54.848 5.426 24.428 1.00 11.74
                                                          PROT
                              56.644 5.131 23.122 1.00 19.57
                                                           PROT
    ATOM 1028 N PHE 354
    ATOM 1029 CA PHE 354
                              57.034 3.944 23.862 1.00 14.42
                                                           PROT
                              58.256 3.270 23.209 1.00 3.70
    ATOM 1030 CB PHE 354
                                                           PROT
20
                              57.890 2.141 22.284 1.00 9.42
    ATOM 1031 CG PHE 354
                                                           PROT
    ATOM 1032 CD1 PHE 354
                               57.427 2.401 20.995 1.00 12.33
                                                            PROT
    ATOM 1033 CD2 PHE 354
                               57.912 0.822 22.727 1.00 15.63
                                                            PROT
                               56.982 1.366 20.165 1.00 6.67
    ATOM 1034 CE1 PHE 354
                                                           PROT
                              57.468 -0.224 21.900 1.00 16.53
                                                           PROT
25
    ATOM 1035 CE2 PHE 354
    ATOM 1036 CZ PHE 354
                              57.002 0.053 20.620 1.00 11.61
                                                           PROT
    ATOM 1037 C PHE 354
                              57.322 4.346 25.307 1.00 18.55
                                                           PROT
                              56.796 3.740 26.233 1.00 16.67
    ATOM 1038 O PHE 354
                                                           PROT
    ATOM 1039 N ASP 355
                              58.125 5.392 25.491 1.00 12.83
                                                           PROT
                             58.486 5.881 26.818 1.00 5.31
                                                           PROT
    ATOM 1040 CA ASP 355
30
    ATOM 1041 CB ASP 355
                              59.351 7.132 26.697 1.00 9.38
                                                           PROT
    ATOM 1042 CG ASP 355
                              60.805 6.814 26.428 1.00 5.96
                                                           PROT
                               61.112 5.683 26.016 1.00 8.53
                                                           PROT
    ATOM 1043 OD1 ASP 355
    ATOM 1044 OD2 ASP 355
                               61.650 7.706 26.628 1.00 15.51
                                                          PROT
                              57.252 6.199 27.659 1.00 10.27
                                                          PROT
35
    ATOM 1045 C ASP 355
                              57.231 5.972 28.871 1.00 21.86
                                                           PROT
    ATOM 1046 O ASP 355
                              56.224 6.726 27.014 1.00 4.18
    ATOM 1047 N LEU 356
                                                          PROT
                             54.988 7.061 27.697 1.00 2.07
    ATOM 1048 CA LEU 356
                                                           PROT
    ATOM 1049 CB LEU 356
                              54.086 7.865 26.771 1.00 2.24
                                                           PROT
                              52.694 8.229 27.266 1.00 3.11
    ATOM 1050 CG LEU 356
                                                           PROT
40
    ATOM 1051 CD1 LEU 356
                               52.771 9.317 28.323 1.00 2.00
                                                           PROT
    ATOM 1052 CD2 LEU 356
                               51.877 8.709 26.086 1.00 2.00
                                                          PROT
    ATOM 1053 C LEU 356
                              54.281 5.786 28.091 1.00 9.17
                                                          PROT
                                                           PROT
    ATOM 1054 O LEU 356
                              53.831 5.644 29.221 1.00 14.77
    ATOM 1055 N GLY 357
                              54.183 4.856 27.147 1.00 13.10
                                                           PROT
45
                              53.515 3.597 27.413 1.00 6.91
                                                           PROT
    ATOM 1056 CA GLY 357
    ATOM 1057 C GLY 357
                              54.113 2.879 28.598 1.00 8.33
                                                          PROT
    ATOM 1058 O GLY 357
                              53.400 2.426 29.492 1.00 9.09
                                                          PROT
    ATOM 1059 N MET 358 55.435 2.768 28.607 1.00 12.61
                                                           PROT
    ATOM 1060 CA MET 358 56.112 2:091 29.692 1.00 10.53
                                                          PROT
50
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57.626 2.153 29.498 1.00 5.45
    ATOM 1061 CB MET 358
                                                            PROT
    ATOM 1062 CG MET 358
                               58.138 1.507 28.210 1.00 15.15
                                                            PROT
                               59.971 1.352 28.113 1.00 17.63
                                                            PROT
    ATOM 1063 SD MET 358
                               60.445 3.023 27.774 1.00 20.56
                                                            PROT
    ATOM 1064 CE MET 358
                              55.714 2.809 30.972 1.00 15.08
                                                           PROT
    ATOM 1065 C MET 358
    ATOM 1066 O MET 358
                              55.241 2.191 31.920 1.00 27.69
                                                           PROT
                              55.875 4.125 30.984 1.00 20.67
                                                           PROT
    ATOM 1067 N SER 359
                              55.551 4.924 32.158 1.00 19.72
                                                           PROT
    ATOM 1068 CA SER 359
    ATOM 1069 CB SER 359
                              55.831 6.398 31.861 1.00 19.98
                                                            PROT
                                                            PROT
                               54.753 7.220 32.262 1.00 33.66
    ATOM 1070 OG SER 359
10
                              54.115 4.757 32.656 1.00 22.67
    ATOM 1071 C SER 359
                                                           PROT
                              53.849 4.837 33.860 1.00 22.94
                                                           PROT
    ATOM 1072 O SER 359
                              53.197 4.514 31.727 1.00 20.55
    ATOM 1073 N LEU 360
                                                           PROT
                               51.785 4.360 32.054 1.00 17.01
                                                           PROT
    ATOM 1074 CA LEU 360
    ATOM 1075 CB LEU 360
                               50.934 4.578 30.802 1.00 2.60
                                                           PROT
15
                               50.674 5.988 30.291 1.00 6.99
                                                            PROT
    ATOM 1076 CG LEU 360
                               49.589 5.935 29.236 1.00 4.15
                                                            PROT
    ATOM 1077 CD1 LEU 360
                               50.247 6.892 31.432 1.00 18.93
                                                           PROT
    ATOM 1078 CD2 LEU 360
                              51.437 3.001 32.638 1.00 19.29
                                                           PROT
    ATOM 1079 C LEU 360
                              50.319 2.802 33.102 1.00 27.53
                                                           PROT
20
    ATOM 1080 O LEU 360
                              52.375 2.061 32.596 1.00 21.73
                                                           PROT
    ATOM 1081 N SER 361
    ATOM 1082 CA SER 361
                               52.139 0.712 33.114 1.00 23.03
                                                            PROT
                               53.415 -0.130 33.027 1.00 25.89
                                                            PROT
    ATOM 1083 CB SER 361
                                                           PROT
                             53.645 -0.613 31.717 1.00 27.77
    ATOM 1084 OG SER 361
    ATOM 1085 C SER 361
                              51.681 0.730 34.563 1.00 23.26
                                                           PROT
25
                              50.720 0.046 34.929 1.00 18.73
                                                           PROT
    ATOM 1086 O SER 361
                              52.388 1.524 35.367 1.00 29.84
                                                           PROT
    ATOM 1087 N SER 362
                              52.141 1.668 36.799 1.00 24.49
                                                            PROT
    ATOM 1088 CA SER 362
                               53.435 2.089 37.491 1.00 26.14
                                                            PROT
    ATOM 1089 CB SER 362
                             53.917 3.305 36.949 1.00 25.03
                                                           PROT
    ATOM 1090 OG SER 362
30
                              51.031 2.635 37.210 1.00 26.86
                                                           PROT
    ATOM 1091 C SER 362
                              50.797 2.831 38.404 1.00 39.63
                                                           PROT
    ATOM 1092 O SER 362
                              50.361 3.251 36.240 1.00 20.94
                                                           PROT
    ATOM 1093 N PHE 363
                               49.272 4.185 36.545 1.00 18.33
                                                           PROT
    ATOM 1094 CA PHE 363
    ATOM 1095 CB PHE 363
                               49.191 5.294 35.486 1.00 17.03
                                                            PROT
35
                               50.171 6.407 35.706 1.00 22.73
                                                            PROT
    ATOM 1096 CG PHE 363
                                                            PROT
                               49.733 7.689 35.990 1.00 9.72
    ATOM 1097 CD1 PHE 363
                               51.545 6.167 35.659 1.00 24.77
                                                            PROT
    ATOM 1098 CD2 PHE 363
                               50.645 8.712 36.225 1.00 16.85
                                                            PROT
    ATOM 1099 CE1 PHE 363
                               52.463 7.198 35.897 1.00 14.26
                                                            PROT
    ATOM 1100 CE2 PHE 363
40
                               52.011 8.462 36.179 1.00 2.26
                                                           PROT
    ATOM 1101 CZ PHE 363
    ATOM 1102 C PHE 363
                              47.958 3.417 36.598 1.00 16.57
                                                           PROT
                              46.971 3.882 37.165 1.00 13.08
                                                           PROT
    ATOM 1103 O PHE 363
                              47.976 2.231 36.002 1.00 17.31
    ATOM 1104 N ASN 364
                                                           PROT
                               46.819 1.349 35.949 1.00 26.11
                                                            PROT
    ATOM 1105 CA ASN 364
45
                               46.673 0.608 37.276 1.00 16.96
                                                            PROT
    ATOM 1106 CB ASN 364
     ATOM 1107 CG ASN 364
                               47.402 -0.715 37.267 1.00 31.34
                                                            PROT
                              46.965 -1.657 36.613 1.00 36.66
                                                             PROT
    ATOM 1108 OD1 ASN 364
                               48.527 -0.794 37.985 1.00 31.61
                                                             PROT
    ATOM 1109 ND2 ASN 364
                              45.527 2.060 35.594 1.00 18.22
                                                           PROT
    ATOM 1110 C ASN 364
50
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44.522 1.923 36.286 1.00 23.17
                                                           PROT
    ATOM 1111 O ASN 364
                              45.567 2.803 34.491 1.00 13.10
    ATOM 1112 N LEU 365
                                                           PROT
    ATOM 1113 CA LEU 365
                              44.417 3.562 34.013 1.00 15.41
                                                            PROT
                              44.833 4.483 32.861 1.00 16.55
                                                            PROT
    ATOM 1114 CB LEU 365
    ATOM 1115 CG LEU 365
                               45.762 5.653 33.181 1.00 19.56
                                                            PROT
    ATOM 1116 CD1 LEU 365
                               46.146 6.373 31.897 1.00 6.69
                                                            PROT
                               45.067 6.602 34.128 1.00 15.69
                                                           PROT
    ATOM 1117 CD2 LEU 365
                              43.328 2.624 33.520 1.00 12.07
                                                           PROT
    ATOM 1118 C LEU 365
    ATOM 1119 O LEU 365
                              43.620 1.534 33.043 1.00 19.81
                                                           PROT
                              42.077 3.047 33.653 1.00 10.86
                                                           PROT
    ATOM 1120 N ASP 366
10
                              40.942 2.263 33.180 1.00 8.96
                                                           PROT
    ATOM 1121 CA ASP 366
                              39.933 2.021 34.326 1.00 9.59
                                                           PROT
    ATOM 1122 CB ASP 366
                                                            PROT
    ATOM 1123 CG ASP 366
                              39.300 3.306 34.859 1.00 21.78
    ATOM 1124 OD1 ASP 366
                               39.871 4.397 34.676 1.00 25.60
                                                            PROT
                               38.217 3.222 35.474 1.00 19.16
                                                            PROT
    ATOM 1125 OD2 ASP 366
15
                             40.288 3.005 32.002 1.00 8.82
                                                          PROT
    ATOM 1126 C ASP 366
                              40.666 4.132 31.681 1.00 17.66
    ATOM 1127 O ASP 366
                                                           PROT
                              39.321 2.379 31.346 1.00 9.45
                                                          PROT
    ATOM 1128 N ASP 367
                              38.668 3.023 30.218 1.00 11.11
    ATOM 1129 CA ASP 367
                                                            PROT
    ATOM 1130 CB ASP 367
                              37.457 2.205 29.769 1.00 20.67
                                                            PROT
20
    ATOM 1131 CG ASP 367
                              37.832 0.812 29.301 1.00 25.02
                                                            PROT
                                                            PROT
    ATOM 1132 OD1 ASP 367
                               39.040 0.525 29.158 1.00 21.06
                               36.909 0.002 29.076 1.00 31.37
                                                           PROT
    ATOM 1133 OD2 ASP 367
                             38.233 4.445 30.574 1.00 14.44
                                                           PROT
    ATOM 1134 C ASP 367
                                                           PROT
25
    ATOM 1135 O ASP 367
                              38.457 5.380 29.815 1.00 26.42
                              37.619 4.612 31.735 1.00 13.62
    ATOM 1136 N THR 368
                                                           PROT
                               37.157 5.926 32.160 1.00 13.14
                                                            PROT
    ATOM 1137 CA THR 368
                                                            PROT
    ATOM 1138 CB THR 368
                               36.510 5.853 33.547 1.00 16.53
    ATOM 1139 OG1 THR 368
                              35.482 4.856 33.550 1.00 10.44
                                                           PROT
                               35.928 7.188 33.925 1.00 5.20
                                                            PROT
    ATOM 1140 CG2 THR 368
30
                              38.291 6.942 32.226 1.00 13.03
                                                           PROT
    ATOM 1141 C THR 368
    ATOM 1142 O THR 368
                              38.114 8.108 31.878 1.00 12.90
                                                           PROT
    ATOM 1143 N GLU 369
                              39.455 6.492 32.686 1.00 9.96
                                                           PROT
                               40.616 7.365 32.821 1.00 7.34
                                                            PROT
    ATOM 1144 CA GLU 369
                                                            PROT
    ATOM 1145 CB GLU 369
                               41.673 6.687 33.708 1.00 10.25
35
                                                            PROT
    ATOM 1146 CG GLU 369
                               41.584 7.113 35.189 1.00 14.56
                               41.599 5.945 36.167 1.00 19.39
    ATOM 1147 CD GLU 369
                                                            PROT
                                                            PROT
                               42.255 4.922 35.864 1.00 19.65
    ATOM 1148 OE1 GLU 369
    ATOM 1149 OE2 GLU 369
                               40.954 6.054 37.233 1.00 7.98
                                                            PROT
                                                           PROT
                              41.203 7.768 31.468 1.00 4.33
40
    ATOM 1150 C GLU 369
                              41.467 8.944 31.213 1.00 7.50
                                                           PROT
    ATOM 1151 O GLU 369
     ATOM 1152 N VAL 370
                              41.406 6.784 30.603 1.00 12.29
                                                           PROT
                               41.927 7.040 29.267 1.00 19.01
                                                            PROT
    ATOM 1153 CA VAL 370
                                                            PROT
    ATOM 1154 CB VAL 370
                               42.092 5.726 28.496 1.00 10.10
    ATOM 1155 CG1 VAL 370
                               42.431 6.011 27.049 1.00 8.57
                                                            PROT
45
                               43.168 4.877 29.159 1.00 12.40
                                                           PROT
    ATOM 1156 CG2 VAL 370
    ATOM 1157 C VAL 370
                              40.896 7.915 28.555 1.00 18.30
                                                           PROT
    ATOM 1158 O VAL 370
                              41.230 8.872 27.855 1.00 17.19
                                                           PROT
                              39.633 7.581 28.760 1.00 2.00
                                                           PROT
    ATOM 1159 N ALA 371
                             38.549 8.321 28.157 1.00 3.53
                                                            PROT
50
    ATOM 1160 CA ALA 371
```

	ATOM	1161 CB ALA 371	37.215 7.728 28.591 1.00 9.17	PROT
	ATOM	1162 C ALA 371	38.603 9.797 28.529 1.00 9.97	PROT
	ATOM	1163 O ALA 371	38.626 10.666 27.655 1.00 24.55	PROT
	ATOM	1164 N LEU 372	38.633 10.082 29.831 1.00 14.85	PROT
5	ATOM	1165 CA LEU 372	38.636 11.463 30.307 1.00 9.24	PROT
	ATOM	1166 CB LEU 372	38.480 11.501 31.830 1.00 8.83	PROT
	ATOM	1167 CG LEU 372	37.043 11.288 32.364 1.00 5.50	PROT
	ATOM	1168 CD1 LEU 372	37.036 10.338 33.553 1.00 2.02	PROT
	ATOM	1169 CD2 LEU 372	36.455 12.626 32.770 1.00 2.00	PROT
10	ATOM	1170 C LEU 372	39.867 12.218 29.870 1.00 10.17	PROT
	ATOM	1171 O LEU 372	39.791 13.413 29.568 1.00 7.23	PROT
	ATOM	1172 N LEU 373	40.996 11.510 29.825 1.00 13.10	PROT
	ATOM	1173 CA LEU 373	42.270 12.078 29.399 1.00 2.00	PROT
	ATOM	1174 CB LEU 373	43.325 10.981 29.381 1.00 2.00	PROT
15	ATOM	1175 CG LEU 373	44.705 11.118 30.045 1.00 9.64	PROT
	ATOM	1176 CD1 LEU 373	44.817 12.382 30.875 1.00 2.00	PROT
	ATOM	1177 CD2 LEU 373	44.955 9.883 30.882 1.00 2.00	PROT
	ATOM	1178 C LEU 373	42.026 12.602 27.987 1.00 6.58	PROT
	ATOM	1179 O LEU 373	42.357 13.738 27.660 1.00 9.73	PROT
20	ATOM	1180 N GLN 374	41.401 11.763 27.165 1.00 9.45	PROT
	ATOM	1181 CA GLN 374	41.076 12.097 25.785 1.00 2.00	PROT
	ATOM	1182 CB GLN 374	40.382 10.914 25.121 1.00 2.00	PROT
	ATOM	1183 CG GLN 374	41.332 9.896 24.537 1.00 2.00	PROT
	ATOM	1184 CD GLN 374	40.630 8.641 24.095 1.00 2.00	PROT
25	ATOM	1185 OE1 GLN 374	41.261 7.622 23.855 1.00 8.01	PROT
	ATOM	1186 NE2 GLN 374	39.316 8.705 23.989 1.00 2.00	PROT
	ATOM	1187 C GLN 374	40.187 13.326 25.694 1.00 2.78	PROT
	ATOM	1188 O GLN 374	40.427 14.213 24.875 1.00 13.91	PROT
20	ATOM	1189 N ALA 375	39.151 13.386 26.521 1.00 2.00	PROT
30	ATOM	1190 CA ALA 375	38.261 14.546 26.505 1.00 2.00	PROT
	ATOM	1191 CB ALA 375	37.128 14.348 27.489 1.00 3.97	PROT
	ATOM	1192 C ALA 375	39.061 15.801 26.868 1.00 4.60	PROT
	ATOM	1193 O ALA 375	38.881 16.864 26.274 1.00 8.82	PROT
2.5	ATOM	1194 N VAL 376	39.956 15.667 27.842 1.00 9.01	PROT
35	ATOM	1195 CA VAL 376	40.772 16.790 28.267 1.00 7.36 41.669 16.401 29.467 1.00 2.30	PROT PROT
	ATOM	1196 CB VAL 376		
			42.597 17.532 29.839 1.00 2.00 40.801 16.076 30.646 1.00 9.15	PROT PROT
	ATOM	1198 CG2 VAL 376 1199 C VAL 376	41.629 17.256 27.110 1.00 3.94	PROT
40		1200 O VAL 376	41.788 18.455 26.880 1.00 2.00	PROT
40		1200 O VAL 370 1201 N LEU 377	42.179 16.297 26.379 1.00 3.92	PROT
		1201 N LEO 377	43.020 16.618 25.239 1.00 5.65	PROT
		1202 CA LEU 377	43.714 15.354 24.731 1.00 5.08	PROT
	ATOM		45.052 15.005 25.386 1.00 2.00	PROT
45	ATOM		45.620 13.790 24.719 1.00 2.00	PROT
73	ATOM	1206 CD2 LEU 377	46.016 16.157 25.264 1.00 4.14	PROT
	ATOM	1200 CD2 EEG 377	42.173 17.271 24.137 1.00 11.35	PROT
	ATOM	1207 C LEU 377	42.607 18.240 23.515 1.00 8.78	PROT
	ATOM	1209 N LEU 378	40.959 16.766 23.912 1.00 5.62	PROT
50		1210 CA LEU 378	40.080 17.352 22.900 1.00 8.57	PROT

```
38.784 16.553 22.788 1.00 5.98
                                                             PROT
    ATOM 1211 CB LEU 378
                                                             PROT
    ATOM 1212 CG LEU 378
                               37.847 16.993 21.658 1.00 6.60
                               38.550 16.826 20.329 1.00 2.00
                                                             PROT
    ATOM 1213 CD1 LEU 378
                                36.563 16.172 21.690 1.00 9.27
                                                             PROT
    ATOM 1214 CD2 LEU 378
                              39.738 18.833 23.146 1.00 10.76
                                                            PROT
    ATOM 1215 C LEU 378
    ATOM 1216 O LEU 378
                              40.045 19.689 22.312 1.00 14.81
                                                            PROT
                               39.106 19.139 24.278 1.00 13.15
                                                             PROT
    ATOM 1217 N MET 379
                                                             PROT
    ATOM 1218 CA MET 379
                               38.735 20.521 24.591 1.00 13.60
    ATOM 1219 CB MET 379
                               37.698 20.543 25.709 1.00 12.57
                                                              PROT
                               36.425 19.782 25.395 1.00 21.12
                                                             PROT
    ATOM 1220 CG MET 379
10
    ATOM 1221 SD MET 379
                               35.533 20.396 23.927 1.00 15.79
                                                             PROT
                               34.397 19.099 23.756 1.00 13.95
                                                             PROT
    ATOM 1222 CE MET 379
                              39.912 21.419 24.988 1.00 16.01
                                                             PROT
    ATOM 1223 C MET 379
    ATOM 1224 O MET 379
                               39.981 21.897 26.121 1.00 16.95
                                                             PROT
                              40.824 21.663 24.048 1.00 12.39
                                                            PROT
15
    ATOM 1225 N SER 380
                               41.984 22.506 24.303 1.00 10.77
                                                             PROT
    ATOM 1226 CA SER 380
                               43.248 21.815 23.810 1.00 8.45
                                                            PROT
    ATOM 1227 CB SER 380
                               43.288 20.487 24.286 1.00 17.27
                                                             PROT
    ATOM 1228 OG SER 380
    ATOM 1229 C SER 380
                              41.825 23.859 23.621 1.00 15.58
                                                            PROT
                              42.125 24.019 22.432 1.00 23.09
                                                            PROT
    ATOM 1230 O SER 380
20
                              41.368 24.837 24.396 1.00 23.65
                                                            PROT
    ATOM 1231 N SER 381
                               41.123 26.187 23.904 1.00 25.18
                                                             PROT
    ATOM 1232 CA SER 381
                               40.449 27.018 25.003 1.00 34.78
    ATOM 1233 CB SER 381
                                                             PROT
                               41.250 27.073 26.170 1.00 37.79
                                                             PROT
    ATOM 1234 OG SER 381
                              42.342 26.940 23.388 1.00 19.38
                                                            PROT
25
    ATOM 1235 C SER 381
    ATOM 1236 O SER 381
                              42.216 28.032 22.850 1.00 28.81
                                                            PROT
                              43.519 26.361 23.523 1.00 11.80
                                                            PROT
    ATOM 1237 N ASP 382
                               44.716 27.057 23.082 1.00 15.78
                                                             PROT
    ATOM 1238 CA ASP 382
                               45.908 26.595 23.909 1.00 33.97
    ATOM 1239 CB ASP 382
                                                             PROT
                               46.069 25.098 23.891 1.00 48.78
                                                             PROT
    ATOM 1240 CG ASP 382
30
                                                              PROT
    ATOM 1241 OD1 ASP 382
                                45.169 24.401 24.406 1.00 45.58
                                                              PROT
    ATOM 1242 OD2 ASP 382
                                47.091 24.620 23.356 1.00 56.52
                              45.037 26.888 21.604 1.00 21.28
                                                            PROT
    ATOM 1243 C ASP 382
    ATOM 1244 O ASP 382
                              45.907 27.585 21.079 1.00 41.91
                                                            PROT
                               44.357 25.971 20.923 1.00 21.81
                                                             PROT
35
    ATOM 1245 N ARG 383
                               44.636 25.773 19.503 1.00 18.95
                                                              PROT
    ATOM 1246 CA ARG 383
                               43.745 24.685 18.921 1.00 8.26
                                                             PROT
    ATOM 1247 CB ARG 383
                               43.580 23.491 19.821 1.00 18.07
                                                              PROT
    ATOM 1248 CG ARG 383
    ATOM 1249 CD ARG 383
                               44.693 22.487 19.610 1.00 11.10
                                                              PROT
                                44.480 21.261 20.378 1.00 20.54
                                                              PROT
    ATOM 1250 NE ARG 383
40
                               45.460 20.462 20.786 1.00 18.25
                                                              PROT
    ATOM 1251 CZ ARG 383
                               45.187 19.365 21.481 1.00 5.24
    ATOM 1252 NH1 ARG 383
                                                              PROT
                                46.717 20.765 20.495 1.00 19.21
                                                              PROT
    ATOM 1253 NH2 ARG 383
                                                             PROT
                               44.420 27.064 18.728 1.00 19.64
    ATOM 1254 C ARG 383
    ATOM 1255 O ARG 383
                               43,493 27.828 19.001 1.00 17.46
                                                             PROT
45
                              45.298 27.342 17.762 1.00 25.37
                                                             PROT
    ATOM 1256 N PRO 384
                               46,485 26.567 17.359 1.00 35.06
                                                             PROT
     ATOM 1257 CD PRO 384
     ATOM 1258 CA PRO 384
                               45.124 28.569 16.983 1.00 27.53
                                                              PROT
                               46.422 28.693 16.181 1.00 18.75
                                                             PROT
    ATOM 1259 CB PRO 384
                               47.041 27.338 16.190 1.00 27.78
                                                              PROT
50
    ATOM 1260 CG PRO 384
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43.895 28.476 16.081 1.00 28.76
                                                            PROT
    ATOM 1261 C PRO 384
                              43.562 27.402 15.560 1.00 31.18
                                                            PROT
    ATOM 1262 O PRO 384
    ATOM 1263 N GLY 385
                              43.215 29.606 15.917 1.00 27.37
                                                            PROT
    ATOM 1264 CA GLY 385
                              42.039 29.638 15.073 1.00 26.98
                                                             PROT
                              40.728 29.442 15.803 1.00 27.46
                                                            PROT
    ATOM 1265 C GLY 385
                              39.689 29.911 15.339 1.00 31.99
                                                            PROT
    ATOM 1266 O GLY 385
                              40.756 28.756 16.939 1.00 34.99
                                                            PROT
    ATOM 1267 N LEU 386
    ATOM 1268 CA LEU 386
                              39.524 28.515 17.673 1.00 37.24
                                                            PROT
                               39.820 27.947 19.059 1.00 26.60
                                                             PROT
    ATOM 1269 CB LEU 386
    ATOM 1270 CG LEU 386
                               40.233 26.472 18.988 1.00 32.45
                                                             PROT
10
                               40.177 25.859 20.363 1.00 34.82
                                                             PROT
    ATOM 1271 CD1 LEU 386
                               39.314 25.719 18.030 1.00 29.64
                                                             PROT
    ATOM 1272 CD2 LEU 386
                              38.733 29.795 17.778 1.00 36.93
                                                            PROT
    ATOM 1273 C LEU 386
                              39.291 30.881 17.674 1.00 37.60
                                                            PROT
    ATOM 1274 O LEU 386
                              37.427 29.665 17.962 1.00 31.47
    ATOM 1275 N ALA 387
                                                            PROT
15
                               36.578 30.832 18.058 1.00 28.80
                                                             PROT
    ATOM 1276 CA ALA 387
    ATOM 1277 CB ALA 387
                               35.553 30.814 16.950 1.00 41.01
                                                             PROT
    ATOM 1278 C ALA 387
                              35.890 30.864 19.400 1.00 28.89
                                                            PROT
                              35.998 31.842 20.133 1.00 30.62
                                                            PROT
    ATOM 1279 O ALA 387
    ATOM 1280 N CYS 388
                              35.167 29.797 19.710 1.00 25.92
                                                            PROT
20
                               34.469 29.712 20.978 1.00 26.90
                                                             PROT
    ATOM 1281 CA CYS 388
    ATOM 1282 CB CYS 388
                               33.224 28.823 20.826 1.00 21.38
                                                             PROT
                               31.625 29.732 20.698 1.00 33.66
                                                             PROT
    ATOM 1283 SG CYS 388
                              35.443 29.159 22.040 1.00 31.18
                                                            PROT
    ATOM 1284 C CYS 388
                              35.272 28.054 22.552 1.00 36.57
                                                            PROT
    ATOM 1285 O CYS 388
25
                              36.473 29.951 22.346 1.00 20.22
                                                            PROT
    ATOM 1286 N VAL 389
    ATOM 1287 CA VAL 389
                               37.511 29.622 23.327 1.00 16.02
                                                             PROT
                               38.554 30.737 23.381 1.00 9.80
                                                             PROT
    ATOM 1288 CB VAL 389
    ATOM 1289 CG1 VAL 389
                                39.526 30.480 24.498 1.00 16.03
                                                              PROT
    ATOM 1290 CG2 VAL 389
                                39.257 30.843 22.056 1.00 16.27
                                                              PROT
30
                              36.977 29.425 24.753 1.00 18.85
                                                            PROT
    ATOM 1291 C VAL 389
    ATOM 1292 O VAL 389
                              37.066 28.336 25.323 1.00 24.21
                                                            PROT
    ATOM 1293 N GLU 390
                              36.461 30.500 25.337 1.00 5.06
                                                            PROT
    ATOM 1294 CA GLU 390
                               35.908 30.434 26.660 1.00 2.00
                                                            PROT
    ATOM 1295 CB GLU 390
                               35.092 31.684 26.952 1.00 5.13
                                                            PROT
35
                              35.047 29.184 26.817 1.00 3.75
                                                            PROT
    ATOM 1296 C GLU 390
                              35.252 28.419 27.754 1.00 23.35
                                                            PROT
    ATOM 1297 O GLU 390
    ATOM 1298 N ARG 391
                               34.103 28.938 25.915 1.00 14.06
                                                            PROT
                                                             PROT
                              33.248 27.754 26.093 1.00 26.18
    ATOM 1299 CA ARG 391
     ATOM 1300 CB ARG 391
                               32.121 27.699 25.049 1.00 31.84
                                                             PROT
40
                               30.843 27.040 25.601 1.00 47.73
                                                             PROT
     ATOM 1301 CG ARG 391
                                29.882 26.572 24.512 1.00 58.24
                                                             PROT
     ATOM 1302 CD ARG 391
     ATOM 1303 NE ARG 391
                               29.879 27.487 23.378 1.00 66.80
                                                             PROT
                                                             PROT
                               29.001 28.470 23.211 1.00 69.56
    ATOM 1304 CZ ARG 391
                                                             PROT
45
    ATOM 1305 NH1 ARG 391
                                29.088 29.255 22.139 1.00 66.99
     ATOM 1306 NH2 ARG 391
                                28.034 28.663 24.105 1.00 56.08
                                                             PROT
                              33.979 26.415 26.110 1.00 23.65
                                                            PROT
     ATOM 1307 C ARG 391
                              33.561 25.479 26.794 1.00 28.58
                                                            PROT
     ATOM 1308 O ARG 391
                             35.064 26.316 25.359 1.00 15.05
     ATOM 1309 N ILE 392
                                                           PROT
                             35.812 25.077 25.335 1.00 19.03
                                                            PROT
    ATOM 1310 CA ILE 392
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PROT
    ATOM 1311 CB ILE 392
                              36.804 25.063 24.165 1.00 22.30
    ATOM 1312 CG2 ILE 392
                              37.971 24.130 24.467 1.00 21.71
                                                             PROT
                               36.074 24.614 22.892 1.00 23.47
                                                             PROT
    ATOM 1313 CG1 ILE 392
                             36.245 25.551 21.707 1.00 4.13
                                                            PROT
    ATOM 1314 CD1 ILE 392
                             36.544 24.907 26.671 1.00 25.03
                                                           PROT
    ATOM 1315 C ILE 392
    ATOM 1316 O ILE 392
                             36.728 23.783 27.153 1.00 26.11
                                                            PROT
    ATOM 1317 N GLU 393
                              36.947 26.029 27.266 1.00 30.74
                                                            PROT
                               37.630 26.021 28.558 1.00 23.39
                                                             PROT
    ATOM 1318 CA GLU 393
    ATOM 1319 CB GLU 393
                               38.073 27.430 28.930 1.00 27.18
                                                             PROT
    ATOM 1320 CG GLU 393
                               39.435 27.817 28.402 1.00 41.39
                                                             PROT
10
                               39.990 29.051 29.093 1.00 47.72
                                                             PROT
    ATOM 1321 CD GLU 393
    ATOM 1322 OE1 GLU 393
                               39.365 29.524 30.070 1.00 39.94
                                                              PROT
    ATOM 1323 OE2 GLU 393
                               41.051 29.547 28.653 1.00 51.17
                                                              PROT
    ATOM 1324 C GLU 393
                              36.655 25.516 29.610 1.00 21.72
                                                             PROT
                              36.942 24.574 30.344 1.00 22.82
    ATOM 1325 O GLU 393
                                                             PROT
15
                              35.497 26.163 29.676 1.00 9.64
    ATOM 1326 N LYS 394
                                                            PROT
    ATOM 1327 CA LYS 394
                               34.462 25.779 30.618 1.00 11.56
                                                             PROT
                               33.177 26.557 30.338 1.00 7.52
    ATOM 1328 CB LYS 394
                                                             PROT
    ATOM 1329 C LYS 394
                              34.213 24.280 30.492 1.00 16.31
                                                            PROT
    ATOM 1330 O LYS 394
                              34.000 23.594 31.498 1.00 24.52
                                                            PROT
20
                              34.251 23.763 29.264 1.00 12.79
    ATOM 1331 N TYR 395
                                                            PROT
    ATOM 1332 CA TYR 395
                               34.033 22.332 29.057 1.00 19.02
                                                             PROT
                               33.803 22.025 27.572 1.00 27.90
                                                             PROT
    ATOM 1333 CB TYR 395
                               32.454 22.456 27.027 1.00 31.64
                                                             PROT
    ATOM 1334 CG TYR 395
                                32.136 22.267 25.684 1.00 30.15
    ATOM 1335 CD1 TYR 395
                                                              PROT
25
                                30.927 22.695 25.160 1.00 28.34
                                                              PROT
    ATOM 1336 CE1 TYR 395
                                31.514 23.085 27.835 1.00 34.21
                                                              PROT
    ATOM 1337 CD2 TYR 395
                               30.298 23.518 27.317 1.00 34.01
                                                              PROT
    ATOM 1338 CE2 TYR 395
    ATOM 1339 CZ TYR 395
                               30.014 23.322 25.979 1.00 33.73
                                                             PROT
                               28.824 23.785 25.453 1.00 44.99
                                                              PROT
    ATOM 1340 OH TYR 395
30
                              35.208 21.490 29.584 1.00 19.03
    ATOM 1341 C TYR 395
                                                             PROT
                              35.003 20.494 30.277 1.00 25.23
                                                             PROT
    ATOM 1342 O TYR 395
                              36.437 21.883 29.256 1.00 17.76
                                                             PROT
    ATOM 1343 N GLN 396
                               37.596 21.134 29.725 1.00 13.73
                                                             PROT
    ATOM 1344 CA GLN 396
    ATOM 1345 CB GLN 396
                               38.905 21.766 29.240 1.00 2.45
                                                             PROT
35
                               40.061 20.767 29.110 1.00 2.00
                                                             PROT
     ATOM 1346 CG GLN 396
     ATOM 1347 CD GLN 396
                               41.388 21.439 28.799 1.00 5.12
                                                             PROT
                                41.706 22.484 29.359 1.00 10.11
                                                             PROT
     ATOM 1348 OE1 GLN 396
                                42.169 20.840 27.903 1.00 9.09
                                                             PROT
     ATOM 1349 NE2 GLN 396
                               37.562 21.149 31.238 1.00 17.65
                                                             PROT
40
     ATOM 1350 C GLN 396
                               37.802 20.125 31.894 1.00 9.63
                                                            PROT
     ATOM 1351 O GLN 396
     ATOM 1352 N ASP 397
                              37.250 22.319 31.787 1.00 6.69
                                                            PROT
                               37.178 22.476 33.226 1.00 9.36
                                                             PROT
     ATOM 1353 CA ASP 397
     ATOM 1354 CB ASP 397
                               36.732 23.893 33.570 1.00 11.44
                                                             PROT
                               37.867 24.891 33.446 1.00 18.32
                                                             PROT
     ATOM 1355 CG ASP 397
45
                                39.033 24.438 33.397 1.00 24.00
                                                              PROT
     ATOM 1356 OD1 ASP 397
     ATOM 1357 OD2 ASP 397
                                37.615 26.114 33.395 1.00 20.67
                                                              PROT
     ATOM 1358 C ASP 397
                              36.215 21.443 33.771 1.00 7.77
                                                            PROT
     ATOM 1359 O ASP 397
                              36.497 20.771 34.761 1.00 7.66
                                                            PROT
                              35.087 21.293 33.093 1.00 9.19
    ATOM 1360 N SER 398
                                                            PROT
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ATOM 1383 C LEU 400 38.527 17.892 36.002 1.00 24.79 PROT ATOM 1384 O LEU 400 39.189 17.228 36.787 1.00 26.46 PROT ATOM 1385 N LEU 401 37.371 18.447 36.354 1.00 21.93 PROT ATOM 1386 CA LEU 401 36.862 18.268 37.707 1.00 17.21 PROT ATOM 1387 CB LEU 401 35.5766 19.285 38.022 1.00 19.27 PROT ATOM 1389 CD1 LEU 401 36.652 20.403 40.085 1.00 2.00 PROT ATOM 1390 CD2 LEU 401 36.316 16.864 37.879 1.00 18.03 PROT ATOM 1392 O LEU 401 36.482 16.250 38.925 1.00 28.63 PROT ATOM 1393 N ALA 402 35.656 16.346 36.856 1.00 9.30 PROT ATOM 1394 CA ALA 402 35.656 16.346 36.856 1.00 9.30 PROT ATOM 1395 CB ALA 402 36.298 14.029 36.989 1.00 7.68 PROT ATOM 1397 O ALA 402 36.298 14.029 36.989 1.00 7.68 PROT ATOM 1398 N PHE 403 37.311 14.305 36.178 1.00 4.49 PROT ATOM 1399 CA PHE 403 38.477 13.439 36.140 1.00 9.18 PROT ATOM 1400 CB PHE 403 39.510 13.977 35.138 1.00 12.80 PROT ATOM 1402 CD1 PHE 403 40.545 12.957 34.693 1.00 5.42 PROT ATOM 1403 CD2 PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1404 CE1 PHE 403 42.546 12.410 33.448 1.00 2.00 PROT ATOM 1405 CE2 PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1407 C PHE 403 39.080 13.366 37.539 1.00 10.08					
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5 ATOM 1366 C SER 398 34.712 18.939 33.556 1.00 11.47 PROT ATOM 1365 O SER 398 34.591 18.227 34.551 1.00 21.11 PROT ATOM 1366 N PHE 399 36.591 18.227 34.551 1.00 21.11 PROT ATOM 1368 CB PHE 399 36.017 17.252 32.417 1.00 24.93 PROT ATOM 1368 CG PHE 399 36.587 17.012 31.014 1.00 23.38 PROT ATOM 1370 CD1 PHE 399 36.587 17.012 31.014 1.00 20.19 PROT ATOM 1371 CD2 PHE 399 35.224 17.638 28.997 1.00 20.19 PROT ATOM 1372 CE1 PHE 399 34.878 15.486 29.988 1.00 8.62 PROT ATOM 1373 CE2 PHE 399 34.975 17.361 28.029 1.00 12.53 PROT ATOM 1374 CZ PHE 399 33.914 15.201 29.027 1.00 19.25 PROT ATOM 1375 C PHE 399 37.113 17.097 33.463 1.00 23.06 PROT ATOM 1376 O PHE 399 37.113 17.097 33.463 1.00 23.06 PROT ATOM 1377 N LEU 400 39.816 19.372 34.461 1.00 10.06 PROT ATOM 1379 CB LEU 400 39.846 19.372 34.461 1.00 10.06 PROT ATOM 1388 CG LEU 400 41.021 19.248 33.491 1.00 8.13 PROT ATOM 1382 CD2 LEU 400 41.021 19.248 33.491 1.00 8.13 PROT ATOM 1388 CD LEU 401 37.371 18.447 36.354 1.00 21.93 PROT ATOM 1386 CA LEU 401 35.766 19.285 38.022 1.00 12.93 PROT ATOM 1390 CD LEU 401 35.766 19.285 38.022 1.00 12.97 PROT ATOM 1390 CD LEU 401 36.652 20.403 40.085 1.00 2.00 PROT ATOM 1390 CD LEU 401 36.652 20.403 40.085 1.00 2.00 PROT ATOM 1390 CD LEU 401 36.652 20.403 40.085 1.00 2.00 PROT ATOM 1390 CD LEU 401 36.652 20.403 40.085 1.00 2.00 PROT ATOM 1390 CD LEU 401 36.652 20.403 40.085 1.00 2.00 PROT ATOM 1390 CD LEU 401 36.652 20.403 40.085 1.00 2.00 PROT ATOM 1390 CD LEU 401 36.652 20.403 40.085 1.00 2.00 PROT ATOM 1390 CD LEU 401 36.462 16.250 38.925 1.00 28.63 PROT ATOM 1390 CD LEU 401 36.462 16.250 38.925 1.00 28.63 PROT ATOM 1390 CD LEU 401 36.462 10.235 39.698 1.00 1.00 5.42 PROT ATOM 1390 CD LEU 401 36.462 10.235 39.698 1.00 1.00 7.03 PROT ATOM 1390 CD LEU 401 36.462 10.235 39.698 1.00 1.00 7.03 PROT ATOM 1390 CD LEU 401 36.462 10.235 39.698 1.00 1.00 9.70 PROT ATOM 1390 CD LEU 401 36.462 10.235 39.698 1.00 1.00 9.70 PROT ATOM 1400 CD PHE 403 40.401 1.004 1.004 1.004 1.004 1.004 1.004 1.004 1.004 1.004 1.004 1.004 1.004 1.004 1.004 1.004 1.0					
5         ATOM         1365         O         SER         398         34.591         18.227         34.551         1.00 21.11         PROT           ATOM         1366         N         PHE         399         35.394         18.565         32.485         1.00 24.93         PROT           ATOM         1368         CB         PHE         399         36.587         17.012         31.014         1.00 24.93         PROT           ATOM         1370         CD1 PHE         399         35.543         16.705         29.981         1.00 20.19         PROT           ATOM         1371         CD2 PHE         399         34.257         17.361         28.997         1.00 22.94         PROT           ATOM         1373         CE2 PHE         399         34.257         17.361         28.029         1.00 12.53         PROT           ATOM         1376         C PHE         399         33.141         15.201         29.027         1.00 19.25         PROT           ATOM         1376         C PHE         399         37.113         17.097         33.463         1.00 23.06         PROT           ATOM         1376         C PHE         399         37.210         16					
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ATOM 1368 CB PHE 399	5	ATOM			
ATOM 1368 CB PHE 399		ATOM	1366 N PHE 399		
ATOM   1369   CG   PHE   399   35.543   16.705   29.981   1.00   20.19   PROT   ATOM   1370   CD1   PHE   399   35.224   17.638   28.997   1.00   22.94   PROT   ATOM   1371   CD2   PHE   399   34.257   17.361   28.029   1.00   12.53   PROT   ATOM   1373   CE2   PHE   399   34.257   17.361   28.029   1.00   12.53   PROT   ATOM   1374   CZ   PHE   399   33.914   15.201   29.027   1.00   19.25   PROT   ATOM   1375   C   PHE   399   37.113   17.097   33.463   1.00   23.06   PROT   ATOM   1376   O   PHE   399   37.210   16.063   34.137   1.00   15.15   PROT   ATOM   1377   N   LEU   400   37.932   18.131   33.604   1.00   22.12   PROT   ATOM   1378   CB   LEU   400   39.017   18.095   34.567   1.00   18.27   PROT   ATOM   1380   CG   LEU   400   41.021   19.248   33.491   1.00   8.13   PROT   ATOM   1381   CD1   LEU   400   41.021   19.248   33.491   1.00   8.13   PROT   ATOM   1384   O   LEU   400   41.021   19.248   33.491   1.00   2.00   PROT   ATOM   1384   O   LEU   400   41.021   19.248   33.491   1.00   2.00   PROT   ATOM   1385   N   LEU   401   38.527   17.892   36.002   1.00   12.79   PROT   ATOM   1385   N   LEU   401   36.862   18.268   37.707   1.00   17.21   PROT   ATOM   1385   CB   LEU   401   36.862   18.268   37.707   1.00   17.21   PROT   ATOM   1389   CD   LEU   401   36.652   20.403   40.085   1.00   2.09   PROT   ATOM   1390   CD   LEU   401   36.482   16.250   38.925   1.00   14.41   PROT   ATOM   1391   C   LEU   401   36.482   16.250   38.925   1.00   2.00   PROT   ATOM   1393   N   ALA   402   36.294   13.054   37.739   1.00   14.41   PROT   ATOM   1396   C   ALA   402   36.294   13.054   37.739   1.00   14.91   PROT   ATOM   1397   C   ALA   402   36.294   13.054   37.739   1.00   14.91   PROT   ATOM   1397   C   ALA   402   36.294   13.054   37.739   1.00   2.00   PROT   ATOM   1397   C   ALA   402   36.295   13.053   36.075   1.00   1.00   PROT   ATOM   1400   CB   PHE   403   40.545   12.957   34.693   1.00   2.00   PROT   ATOM   1400   CB   PHE   403   40.545   12.957   34.661   1.00		ATOM	1367 CA PHE 399	36.017 17.252 32.417 1.00 24.93	PROT
10 ATOM 1370 CD1 PHE 399 35.224 17.638 28.997 1.00 22.94 PROT ATOM 1371 CD2 PHE 399 34.878 15.486 29.988 1.00 8.62 PROT ATOM 1373 CE2 PHE 399 34.257 17.361 28.029 1.00 12.53 PROT ATOM 1373 CE2 PHE 399 33.914 15.201 29.027 1.00 19.25 PROT ATOM 1375 C PHE 399 33.604 16.143 28.044 1.00 15.15 PROT ATOM 1376 O PHE 399 37.113 17.097 33.463 1.00 23.06 PROT ATOM 1377 N LEU 400 37.932 18.131 33.604 1.00 22.12 PROT ATOM 1377 N LEU 400 37.932 18.131 33.604 1.00 22.12 PROT ATOM 1378 CA LEU 400 39.816 19.372 34.461 1.00 10.06 PROT ATOM 1380 CG LEU 400 41.021 19.248 33.491 1.00 8.13 PROT ATOM 1382 CD2 LEU 400 42.055 18.333 34.095 1.00 13.73 PROT ATOM 1383 C LEU 400 39.189 17.228 36.787 1.00 24.79 PROT ATOM 1385 N LEU 401 37.371 18.447 36.354 1.00 24.79 PROT ATOM 1386 CA LEU 401 37.371 18.447 36.354 1.00 21.93 PROT ATOM 1387 CB LEU 401 35.766 19.285 38.022 1.00 24.79 PROT ATOM 1388 CG LEU 401 35.766 19.285 38.022 1.00 19.27 PROT ATOM 1389 CD1 LEU 401 35.766 19.285 38.022 1.00 19.27 PROT ATOM 1389 CD2 LEU 401 35.566 19.285 38.022 1.00 19.27 PROT ATOM 1390 CD2 LEU 401 36.652 20.403 40.085 1.00 2.00 PROT ATOM 1390 CD2 LEU 401 36.466 37.879 1.00 14.41 PROT ATOM 1394 CA ALA 402 36.298 14.029 36.989 1.00 7.68 PROT ATOM 1395 CB ALA 402 36.298 14.029 36.989 1.00 7.68 PROT ATOM 1399 CA PHE 403 38.477 13.439 36.140 1.00 9.18 PROT ATOM 1399 CA PHE 403 38.477 13.439 36.140 1.00 9.18 PROT ATOM 1399 CA PHE 403 38.477 13.439 36.140 1.00 9.18 PROT ATOM 1400 CB PHE 403 40.545 12.957 34.693 1.00 2.00 PROT ATOM 1400 CD1 PHE 403 40.545 12.957 34.693 1.00 2.00 PROT ATOM 1400 CD2 PHE 403 40.545 12.957 34.693 1.00 2.00 PROT ATOM 1403 CD2 PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1403 CD2 PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1405 CD2 PHE 403 41.440 10.711 34.688 1.00 2.00 PROT ATOM 1405 CD2 PHE 403 42.468 11.100 33.468 1.00 2.00 PROT ATOM 1407 C PHE 403 42.468 11.100 33.468 1.00 2.00 PROT ATOM 1407 C PHE 403 42.468 11.100 33.468 1.00 2.00 PROT ATOM 1407 C PHE 403 42.468 11.100 33.366 37.599 1.00 10.08		ATOM	1368 CB PHE 399	36.587 17.012 31.014 1.00 23.38	PROT
ATOM 1371 CD2 PHE 399 34.878 15.486 29.988 1.00 8.62 PROT ATOM 1372 CE1 PHE 399 34.257 17.361 28.029 1.00 12.53 PROT ATOM 1373 CE2 PHE 399 33.914 15.201 29.027 1.00 19.25 PROT ATOM 1374 CZ PHE 399 33.604 16.143 28.044 1.00 15.15 PROT ATOM 1376 C PHE 399 37.113 17.097 33.463 1.00 23.06 PROT ATOM 1376 C PHE 399 37.210 16.063 34.137 1.00 15.58 PROT ATOM 1377 N LEU 400 37.932 18.131 33.604 1.00 22.12 PROT ATOM 1378 CA LEU 400 39.017 18.095 34.567 1.00 18.27 PROT ATOM 1378 CA LEU 400 39.846 19.372 34.461 1.00 10.06 PROT ATOM 1380 CG LEU 400 41.021 19.248 33.491 1.00 8.13 PROT ATOM 1381 CD1 LEU 400 41.021 19.248 33.491 1.00 20.00 PROT ATOM 1382 CD2 LEU 400 42.055 18.333 34.095 1.00 13.73 PROT ATOM 1385 N LEU 401 37.371 18.447 36.354 1.00 21.93 PROT ATOM 1386 CA LEU 401 36.862 18.268 37.707 1.00 17.21 PROT ATOM 1388 CG LEU 401 35.736 19.285 38.022 1.00 19.27 PROT ATOM 1389 CD1 LEU 401 35.766 19.285 38.022 1.00 19.27 PROT ATOM 1389 CD1 LEU 401 36.482 16.250 38.925 1.00 2.00 PROT ATOM 1390 CD2 LEU 401 36.482 16.250 38.925 1.00 2.00 PROT ATOM 1393 N ALA 402 36.286 16.346 36.856 1.00 2.00 PROT ATOM 1394 CA ALA 402 36.294 13.054 36.895 1.00 14.15 PROT ATOM 1396 C ALA 402 36.294 13.054 37.39 1.00 10.00 PROT ATOM 1397 C ALA 402 36.294 13.054 37.39 1.00 2.00 PROT ATOM 1398 N PHE 403 37.311 14.305 36.178 1.00 4.49 PROT ATOM 1399 CA PHE 403 37.311 14.305 36.178 1.00 2.00 PROT ATOM 1399 CA PHE 403 37.311 14.305 36.178 1.00 2.00 PROT ATOM 1400 CB PHE 403 40.546 11.00 33.448 1.00 2.00 PROT ATOM 1400 CD PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1403 CD2 PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1403 CD2 PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1405 CE2 PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1407 C PHE 403 42.648 11.100 33.863 1.00 2.00 PROT ATOM 1407 C PHE 403 42.648 11.100 33.863 1.00 2.00 PROT ATOM 1407 C PHE 403 42.648 11.100 33.863 1.00 2.00 PROT ATOM 1407 C PHE 403 42.648 11.100 33.863 1.00 2.00 PROT ATOM 1407 C PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1407 C PHE 403 42.468 11.100 33.863		ATOM	1369 CG PHE 399	35.543 16.705 29.981 1.00 20.19	PROT
ATOM 1372 CE1 PHE 399 34.257 17.361 28.029 1.00 12.53 PROT ATOM 1373 CE2 PHE 399 33.914 15.201 29.027 1.00 19.25 PROT ATOM 1374 CZ PHE 399 33.604 16.143 28.044 1.00 15.15 PROT ATOM 1375 C PHE 399 37.113 17.097 33.463 1.00 23.06 PROT ATOM 1376 O PHE 399 37.210 16.063 34.137 1.00 15.58 PROT ATOM 1377 N LEU 400 37.932 18.131 33.604 1.00 22.12 PROT ATOM 1378 CA LEU 400 39.846 19.372 34.461 1.00 10.06 PROT ATOM 1380 CG LEU 400 41.021 19.248 33.491 1.00 8.13 PROT ATOM 1381 CD1 LEU 400 41.616 20.594 33.195 1.00 2.00 PROT ATOM 1382 CD2 LEU 400 42.055 18.333 34.095 1.00 13.73 PROT ATOM 1383 C LEU 400 38.827 17.892 36.002 1.00 24.79 PROT ATOM 1385 N LEU 401 37.371 18.447 36.354 1.00 21.93 PROT ATOM 1386 CA LEU 401 35.766 19.285 38.022 1.00 19.27 PROT ATOM 1388 CG LEU 401 35.766 19.285 38.022 1.00 19.27 PROT ATOM 1389 CD1 LEU 401 36.862 18.268 37.707 1.00 17.21 PROT ATOM 1390 CD2 LEU 401 36.862 18.268 37.707 1.00 17.21 PROT ATOM 1390 CD2 LEU 401 36.482 16.250 38.925 1.00 28.63 PROT ATOM 1393 N ALA 402 36.565 16.346 36.856 1.00 2.00 PROT ATOM 1394 CA ALA 402 36.298 14.029 36.989 1.00 7.68 PROT ATOM 1395 CB ALA 402 36.298 14.029 36.989 1.00 7.68 PROT ATOM 1399 CA PHE 403 37.311 14.305 36.178 1.00 2.00 PROT ATOM 1399 CA PHE 403 37.311 14.305 36.178 1.00 2.00 PROT ATOM 1399 CA PHE 403 38.477 13.439 36.140 1.00 9.18 PROT ATOM 1400 CB PHE 403 40.545 12.957 34.693 1.00 2.00 PROT ATOM 1400 CD PHE 403 40.545 12.957 34.693 1.00 2.00 PROT ATOM 1400 CD PHE 403 40.545 12.957 34.693 1.00 2.00 PROT ATOM 1400 CD PHE 403 40.545 12.957 34.693 1.00 2.00 PROT ATOM 1400 CD PHE 403 40.545 12.957 34.693 1.00 2.00 PROT ATOM 1400 CD PHE 403 40.545 12.957 34.693 1.00 2.00 PROT ATOM 1400 CD PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1400 CD PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1400 CD PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1400 CD PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1407 C PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1407 C PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1407 C PHE 403 42.468 11.100 33.	10	ATOM	1370 CD1 PHE 399	35.224 17.638 28.997 1.00 22.94	PROT
ATOM 1373 CE2 PHE 399 33.914 15.201 29.027 1.00 19.25 PROT ATOM 1374 CZ PHE 399 37.113 17.097 33.463 1.00 23.06 PROT ATOM 1375 C PHE 399 37.113 17.097 33.463 1.00 23.06 PROT ATOM 1376 O PHE 399 37.210 16.063 34.137 1.00 15.58 PROT ATOM 1377 N LEU 400 37.932 18.131 33.604 1.00 22.12 PROT ATOM 1378 CA LEU 400 39.846 19.372 34.461 1.00 10.06 PROT ATOM 1380 CG LEU 400 41.021 19.248 33.491 1.00 8.13 PROT ATOM 1381 CD1 LEU 400 41.021 19.248 33.491 1.00 10.06 PROT ATOM 1383 C LEU 400 39.886 19.372 34.461 1.00 10.06 PROT ATOM 1383 C LEU 400 41.021 19.248 33.491 1.00 2.00 PROT ATOM 1383 C LEU 400 39.189 17.228 36.002 1.00 24.79 PROT ATOM 1384 O LEU 400 39.189 17.228 36.002 1.00 24.79 PROT ATOM 1385 N LEU 401 37.371 18.447 36.354 1.00 21.93 PROT ATOM 1386 CA LEU 401 35.7361 18.447 36.354 1.00 21.93 PROT ATOM 1388 CG LEU 401 35.538 19.547 39.515 1.00 10.9.27 PROT ATOM 1389 CD1 LEU 401 36.462 18.268 37.707 1.00 17.21 PROT ATOM 1390 CD2 LEU 401 36.462 20.235 39.687 1.00 14.41 PROT ATOM 1391 C LEU 401 36.365 16.364 37.879 1.00 18.03 PROT ATOM 1393 N ALA 402 36.482 16.250 38.925 1.00 28.63 PROT ATOM 1394 CA ALA 402 35.565 16.346 36.856 1.00 9.30 PROT ATOM 1394 CA ALA 402 36.298 14.029 36.989 1.00 7.68 PROT ATOM 1398 N PHE 403 37.311 14.305 36.178 1.00 4.49 PROT ATOM 1398 N PHE 403 37.311 14.305 36.178 1.00 4.49 PROT ATOM 1398 N PHE 403 37.311 14.305 36.178 1.00 4.49 PROT ATOM 1398 N PHE 403 37.311 14.305 36.178 1.00 2.00 PROT ATOM 1400 CB PHE 403 40.545 12.957 34.693 1.00 2.00 PROT ATOM 1401 CG PHE 403 40.545 12.957 34.693 1.00 2.00 PROT ATOM 1402 CD1 PHE 403 40.545 12.957 34.693 1.00 2.00 PROT ATOM 1403 CD2 PHE 403 40.545 12.957 34.693 1.00 2.00 PROT ATOM 1404 CE1 PHE 403 40.546 12.410 33.448 1.00 2.00 PROT ATOM 1405 CE2 PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1406 CZ PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1406 CZ PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1406 CZ PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1406 CZ PHE 403 40.480 11.364 37.539 1.00 10.08 PROT ATOM 1406 CZ PHE 403 40.480 11.364 3		ATOM	1371 CD2 PHE 399	34.878 15.486 29.988 1.00 8.62	PROT
ATOM 1374 CZ PHE 399 33.604 16.143 28.044 1.00 15.15 PROT ATOM 1375 C PHE 399 37.113 17.097 33.463 1.00 23.06 PROT ATOM 1376 O PHE 399 37.210 16.063 34.137 1.00 15.58 PROT ATOM 1377 N LEU 400 37.932 18.131 33.604 1.00 22.12 PROT ATOM 1378 CA LEU 400 39.017 18.095 34.567 1.00 18.27 PROT ATOM 1379 CB LEU 400 39.846 19.372 34.461 1.00 10.06 PROT ATOM 1380 CG LEU 400 41.021 19.248 33.491 1.00 8.13 PROT ATOM 1381 CD1 LEU 400 42.055 18.333 34.095 1.00 2.00 PROT ATOM 1383 C LEU 400 39.189 17.228 36.787 1.00 24.79 PROT ATOM 1384 O LEU 400 39.189 17.228 36.787 1.00 26.46 PROT ATOM 1385 N LEU 401 37.371 18.447 36.354 1.00 21.93 PROT ATOM 1386 CA LEU 401 35.766 19.285 38.022 1.00 19.27 PROT ATOM 1389 CD1 LEU 401 35.538 19.547 39.515 1.00 16.76 PROT ATOM 1390 CD2 LEU 401 36.482 16.250 38.925 1.00 22.00 PROT ATOM 1391 C LEU 401 36.482 16.250 38.925 1.00 28.63 PROT ATOM 1393 N ALA 402 36.542 16.250 38.925 1.00 28.63 PROT ATOM 1396 C ALA 402 36.294 13.054 37.739 1.00 7.03 PROT ATOM 1396 C ALA 402 36.294 13.054 37.739 1.00 7.68 PROT ATOM 1397 O ALA 402 36.294 13.054 37.739 1.00 2.00 PROT ATOM 1399 CA PHE 403 39.510 13.397 35.138 1.00 12.00 PROT ATOM 1399 CA PHE 403 39.510 13.397 35.138 1.00 12.00 PROT ATOM 1400 CD PHE 403 40.545 12.957 34.693 1.00 2.00 PROT ATOM 1400 CD PHE 403 40.545 12.957 34.693 1.00 2.00 PROT ATOM 1400 CD PHE 403 40.545 12.957 34.693 1.00 2.00 PROT ATOM 1400 CD PHE 403 40.545 12.957 34.693 1.00 2.00 PROT ATOM 1400 CD PHE 403 40.545 12.957 34.693 1.00 2.00 PROT ATOM 1400 CD PHE 403 40.545 12.957 34.693 1.00 2.00 PROT ATOM 1404 CE PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.546 12.410 33.448 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.546 12.410 33.448 1.00 2.00 PROT ATOM 1406 CZ PHE 403 39.080 13.366 37.539 1.00 10.08 PROT ATOM 1407 C PHE 403 39.080 13.366 37.539 1.00 10.08 PROT ATOM 1407 C PHE 403 39.080 13.366 37.539 1.00 10.08		ATOM	1372 CE1 PHE 399	34.257 17.361 28.029 1.00 12.53	PROT
15 ATOM 1375 C PHE 399 37.113 17.097 33.463 1.00 23.06 PROT ATOM 1376 O PHE 399 37.210 16.063 34.137 1.00 15.58 PROT ATOM 1377 N LEU 400 37.932 18.131 33.604 1.00 22.12 PROT ATOM 1378 CA LEU 400 39.017 18.095 34.567 1.00 18.27 PROT ATOM 1380 CG LEU 400 41.021 19.248 33.491 1.00 8.13 PROT ATOM 1381 CD1 LEU 400 41.021 19.248 33.491 1.00 8.13 PROT ATOM 1382 CD2 LEU 400 42.055 18.333 34.095 1.00 13.73 PROT ATOM 1383 C LEU 400 39.189 17.228 36.002 1.00 24.79 PROT ATOM 1384 O LEU 400 39.189 17.228 36.002 1.00 24.79 PROT ATOM 1385 N LEU 401 37.371 18.447 36.354 1.00 21.93 PROT ATOM 1386 CA LEU 401 35.766 19.285 38.022 1.00 19.27 PROT ATOM 1388 CG LEU 401 35.538 19.547 39.515 1.00 16.76 PROT ATOM 1390 CD2 LEU 401 36.482 16.250 38.925 1.00 28.63 PROT ATOM 1390 CD2 LEU 401 36.482 16.250 38.925 1.00 28.63 PROT ATOM 1394 CA ALA 402 36.246 16.346 36.856 1.00 9.30 PROT ATOM 1396 C ALA 402 36.294 13.054 37.739 1.00 14.15 PROT ATOM 1396 C ALA 402 36.294 13.054 37.739 1.00 14.05 PROT ATOM 1396 C ALA 402 36.294 13.054 37.739 1.00 2.00 PROT ATOM 1399 CA PHE 403 39.510 13.977 35.138 1.00 12.80 PROT ATOM 1399 CA PHE 403 39.510 13.977 35.138 1.00 12.80 PROT ATOM 1400 CB PHE 403 40.545 12.957 34.693 1.00 2.00 PROT ATOM 1400 CB PHE 403 40.545 12.957 34.693 1.00 2.00 PROT ATOM 1402 CD1 PHE 403 40.545 12.957 34.693 1.00 2.00 PROT ATOM 1402 CD1 PHE 403 40.545 12.957 34.693 1.00 2.00 PROT ATOM 1404 CE1 PHE 403 40.546 12.410 33.448 1.00 2.00 PROT ATOM 1404 CE2 PHE 403 40.546 12.410 33.448 1.00 2.00 PROT ATOM 1404 CE2 PHE 403 40.546 12.410 33.448 1.00 2.00 PROT ATOM 1406 CZ PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.546 12.410 33.448 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.546 12.410 33.448 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.546 12.410 33.448 1.00 2.00 PROT ATOM 1406 CZ PHE 403 39.080 13.366 37.539 1.00 10.08 PROT ATOM 1407 C PHE 403 39.080 13.366 37.539 1.00 10.08		ATOM	1373 CE2 PHE 399	33.914 15.201 29.027 1.00 19.25	PROT
ATOM 1376 O PHE 399 37.210 16.063 34.137 1.00 15.58 PROT ATOM 1377 N LEU 400 37.932 18.131 33.604 1.00 22.12 PROT ATOM 1378 CA LEU 400 39.017 18.095 34.567 1.00 18.27 PROT ATOM 1379 CB LEU 400 41.021 19.248 33.491 1.00 8.13 PROT ATOM 1381 CD1 LEU 400 41.021 19.248 33.491 1.00 8.13 PROT ATOM 1382 CD2 LEU 400 42.055 18.333 34.095 1.00 13.73 PROT ATOM 1383 C LEU 400 39.189 17.228 36.787 1.00 26.46 PROT ATOM 1385 N LEU 401 37.371 18.447 36.354 1.00 21.93 PROT ATOM 1386 CA LEU 401 35.538 19.547 39.515 1.00 19.27 PROT ATOM 1388 CG LEU 401 35.538 19.547 39.515 1.00 19.27 PROT ATOM 1389 CD1 LEU 401 36.652 20.403 40.085 1.00 2.00 PROT ATOM 1390 CD2 LEU 401 36.482 16.250 38.925 1.00 18.03 PROT ATOM 1395 CB ALA 402 35.656 16.346 36.856 1.00 9.30 PROT ATOM 1395 CB ALA 402 36.294 13.054 37.739 1.00 2.00 PROT ATOM 1396 C ALA 402 36.294 13.054 37.739 1.00 2.00 PROT ATOM 1396 C ALA 402 36.294 13.054 37.739 1.00 2.00 PROT ATOM 1396 C PROT ATOM 1396 C PROT ATOM 1397 O ALA 402 36.294 13.054 37.739 1.00 2.00 PROT ATOM 1390 CD PROT ATOM 1396 C PROT ATOM 1397 O ALA 402 36.294 13.054 37.739 1.00 2.00 PROT ATOM 1390 CD PROT ATOM 1396 C PROT ATOM 1397 O ALA 402 36.294 13.054 37.739 1.00 2.00 PROT ATOM 1390 CD PROT ATOM 1397 O ALA 402 36.294 13.054 37.739 1.00 2.00 PROT ATOM 1390 CD PROT ATOM 1397 O ALA 402 36.294 13.054 37.739 1.00 2.00 PROT ATOM 1400 CB PHE 403 37.311 14.305 36.178 1.00 4.49 PROT ATOM 1400 CB PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1402 CD1 PHE 403 40.545 12.957 34.693 1.00 5.42 PROT ATOM 1402 CD1 PHE 403 40.545 12.957 34.693 1.00 5.42 PROT ATOM 1406 CZ PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1406 CZ PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.546 12.410 33.468 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.546 12.410 33.468 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.668 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.668 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.668 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.668 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403		ATOM	1374 CZ PHE 399	33.604 16.143 28.044 1.00 15.15	PROT
ATOM 1377 N LEU 400 37.932 18.131 33.604 1.00 22.12 PROT ATOM 1378 CA LEU 400 39.017 18.095 34.567 1.00 18.27 PROT ATOM 1379 CB LEU 400 39.846 19.372 34.461 1.00 10.06 PROT ATOM 1381 CD1 LEU 400 41.021 19.248 33.491 1.00 8.13 PROT ATOM 1382 CD2 LEU 400 42.055 18.333 34.095 1.00 13.73 PROT ATOM 1383 C LEU 400 39.189 17.228 36.002 1.00 24.79 ATOM 1384 O LEU 400 39.189 17.228 36.787 1.00 26.46 PROT ATOM 1386 CA LEU 401 36.862 18.268 37.707 1.00 17.21 PROT ATOM 1387 CB LEU 401 35.731 18.447 36.354 1.00 21.93 PROT ATOM 1388 CG LEU 401 35.538 19.547 39.515 1.00 16.76 PROT ATOM 1389 CD1 LEU 401 36.652 20.403 40.085 1.00 2.00 PROT ATOM 1390 CD2 LEU 401 36.482 16.250 38.925 1.00 28.63 PROT ATOM 1394 CA ALA 402 35.656 16.346 36.856 1.00 9.30 PROT ATOM 1394 CA ALA 402 35.656 16.346 36.856 1.00 9.30 PROT ATOM 1395 CB ALA 402 36.294 13.054 37.739 1.00 14.15 PROT ATOM 1398 N PHE 403 37.311 14.305 36.178 1.00 14.9 PROT ATOM 1399 CA PHE 403 38.477 13.439 36.140 1.00 9.18 PROT ATOM 1400 CB PHE 403 39.510 13.977 35.138 1.00 1.20 PROT ATOM 1401 CG PHE 403 40.545 12.957 34.693 1.00 5.42 PROT ATOM 1402 CD1 PHE 403 40.545 12.957 34.693 1.00 5.42 PROT ATOM 1406 CE PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1406 CZ PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1406 CZ PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.	15	ATOM	1375 C PHE 399	37.113 17.097 33.463 1.00 23.06	PROT
ATOM 1377 N LEU 400 37.932 18.131 33.604 1.00 22.12 PROT ATOM 1378 CA LEU 400 39.017 18.095 34.567 1.00 18.27 PROT ATOM 1379 CB LEU 400 39.846 19.372 34.461 1.00 10.06 PROT ATOM 1381 CD1 LEU 400 41.021 19.248 33.491 1.00 8.13 PROT ATOM 1382 CD2 LEU 400 42.055 18.333 34.095 1.00 13.73 PROT ATOM 1383 C LEU 400 39.189 17.228 36.002 1.00 24.79 ATOM 1384 O LEU 400 39.189 17.228 36.787 1.00 26.46 PROT ATOM 1386 CA LEU 401 36.862 18.268 37.707 1.00 17.21 PROT ATOM 1387 CB LEU 401 35.731 18.447 36.354 1.00 21.93 PROT ATOM 1388 CG LEU 401 35.538 19.547 39.515 1.00 16.76 PROT ATOM 1389 CD1 LEU 401 36.652 20.403 40.085 1.00 2.00 PROT ATOM 1390 CD2 LEU 401 36.482 16.250 38.925 1.00 28.63 PROT ATOM 1394 CA ALA 402 35.656 16.346 36.856 1.00 9.30 PROT ATOM 1394 CA ALA 402 35.656 16.346 36.856 1.00 9.30 PROT ATOM 1395 CB ALA 402 36.294 13.054 37.739 1.00 14.15 PROT ATOM 1398 N PHE 403 37.311 14.305 36.178 1.00 14.9 PROT ATOM 1399 CA PHE 403 38.477 13.439 36.140 1.00 9.18 PROT ATOM 1400 CB PHE 403 39.510 13.977 35.138 1.00 1.20 PROT ATOM 1401 CG PHE 403 40.545 12.957 34.693 1.00 5.42 PROT ATOM 1402 CD1 PHE 403 40.545 12.957 34.693 1.00 5.42 PROT ATOM 1406 CE PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1406 CZ PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1406 CZ PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.		ATOM	1376 O PHE 399	37.210 16.063 34.137 1.00 15.58	PROT
ATOM 1378 CA LEU 400 39.017 18.095 34.567 1.00 18.27 PROT ATOM 1379 CB LEU 400 39.846 19.372 34.461 1.00 10.06 PROT ATOM 1380 CG LEU 400 41.021 19.248 33.491 1.00 8.13 PROT ATOM 1381 CD1 LEU 400 41.616 20.594 33.195 1.00 2.00 PROT ATOM 1383 C LEU 400 42.055 18.333 34.095 1.00 13.73 PROT ATOM 1384 O LEU 400 39.189 17.228 36.002 1.00 24.79 PROT ATOM 1385 N LEU 401 37.371 18.447 36.354 1.00 21.93 PROT ATOM 1386 CA LEU 401 36.862 18.268 37.707 1.00 17.21 PROT ATOM 1388 CG LEU 401 35.766 19.285 38.022 1.00 19.27 PROT ATOM 1389 CD1 LEU 401 35.766 19.285 38.022 1.00 19.27 PROT ATOM 1389 CD1 LEU 401 36.652 20.403 40.085 1.00 2.00 PROT ATOM 1390 CD2 LEU 401 36.316 16.864 37.879 1.00 14.41 PROT ATOM 1391 C LEU 401 36.316 16.864 37.879 1.00 14.41 PROT ATOM 1393 N ALA 402 35.656 16.346 36.856 1.00 9.30 PROT ATOM 1394 CA ALA 402 35.656 16.346 36.856 1.00 9.30 PROT ATOM 1395 CB ALA 402 35.656 16.346 36.856 1.00 9.30 PROT ATOM 1396 C ALA 402 36.294 13.054 37.739 1.00 14.15 PROT ATOM 1397 O ALA 402 36.294 13.054 37.739 1.00 14.15 PROT ATOM 1399 CA PHE 403 37.311 14.305 36.178 1.00 4.49 PROT ATOM 1399 CA PHE 403 38.477 13.439 36.140 1.00 9.18 PROT ATOM 1400 CB PHE 403 39.510 13.977 35.138 1.00 12.80 PROT ATOM 1402 CD1 PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1402 CD1 PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1404 CE2 PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.546 12.410 33.448 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.546 12.410 33.468 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.546 12.410 33.468 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.546 11.100 33.865 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.546 11.101 33.866 37.539 1.00 10.08 PROT ATOM 1407 C PHE 403 39.080 13.366 37.539 1.00 10.08		ATOM	1377 N LEU 400		PROT
ATOM 1379 CB LEU 400 39.846 19.372 34.461 1.00 10.06 PROT ATOM 1381 CD1 LEU 400 41.021 19.248 33.491 1.00 8.13 PROT ATOM 1382 CD2 LEU 400 42.055 18.333 34.095 1.00 2.00 PROT ATOM 1384 O LEU 400 39.189 17.228 36.002 1.00 24.79 PROT ATOM 1385 N LEU 401 37.371 18.447 36.354 1.00 21.93 PROT ATOM 1386 CA LEU 401 36.862 18.268 37.707 1.00 17.21 PROT ATOM 1387 CB LEU 401 35.538 19.547 39.515 1.00 16.76 PROT ATOM 1389 CD1 LEU 401 36.652 20.403 40.085 1.00 2.00 PROT ATOM 1390 CD2 LEU 401 36.482 16.250 38.925 1.00 18.03 PROT ATOM 1393 N ALA 402 36.482 16.250 38.925 1.00 28.63 PROT ATOM 1394 CA ALA 402 35.656 16.346 36.856 1.00 9.30 PROT ATOM 1395 CB ALA 402 35.656 16.346 36.856 1.00 9.30 PROT ATOM 1396 C ALA 402 35.656 16.346 36.856 1.00 9.30 PROT ATOM 1399 N PHE 403 37.311 14.305 36.178 1.00 14.15 PROT ATOM 1399 CD LEU 401 36.294 13.054 37.739 1.00 2.00 PROT ATOM 1399 C ALA 402 36.294 13.054 37.739 1.00 2.00 PROT ATOM 1399 C ALA 402 36.294 13.054 37.739 1.00 2.00 PROT ATOM 1399 C ALA 402 36.294 13.054 37.739 1.00 2.00 PROT ATOM 1399 C A PHE 403 37.311 14.305 36.178 1.00 4.49 PROT ATOM 1400 CB PHE 403 39.510 13.977 35.138 1.00 12.80 PROT ATOM 1400 CB PHE 403 39.510 13.977 35.138 1.00 12.80 PROT ATOM 1400 CD1 PHE 403 40.545 12.957 34.693 1.00 2.00 PROT ATOM 1404 CE1 PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1405 CE2 PHE 403 42.468 11.100 33.868 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.868 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.868 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.868 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.868 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.868 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.868 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.868 1.00 2.00 PROT ATOM 1407 C PHE 403 39.080 13.366 37.539 1.00 10.08		ATOM	1378 CA LEU 400		PROT
ATOM 1381 CD1 LEU 400		ATOM	1379 CB LEU 400	39.846 19.372 34.461 1.00 10.06	PROT
ATOM 1382 CD2 LEU 400	20	ATOM	1380 CG LEU 400	41.021 19.248 33.491 1.00 8.13	PROT
ATOM 1383 C LEU 400 38.527 17.892 36.002 1.00 24.79 PROT ATOM 1384 O LEU 400 39.189 17.228 36.787 1.00 26.46 PROT ATOM 1385 N LEU 401 37.371 18.447 36.354 1.00 21.93 PROT ATOM 1387 CB LEU 401 36.862 18.268 37.707 1.00 17.21 PROT ATOM 1388 CG LEU 401 35.538 19.547 39.515 1.00 16.76 PROT ATOM 1390 CD2 LEU 401 36.352 20.403 40.085 1.00 2.00 PROT ATOM 1391 C LEU 401 36.482 16.250 38.925 1.00 18.03 PROT ATOM 1392 O LEU 401 36.482 16.250 38.925 1.00 28.63 PROT ATOM 1394 CA ALA 402 35.656 16.346 36.856 1.00 9.30 PROT ATOM 1395 CB ALA 402 35.656 16.346 36.856 1.00 9.30 PROT ATOM 1396 C ALA 402 36.298 14.029 36.989 1.00 7.68 PROT ATOM 1398 N PHE 403 37.311 14.305 36.178 1.00 4.49 PROT ATOM 1399 CA PHE 403 38.477 13.439 36.140 1.00 9.18 PROT ATOM 1400 CB PHE 403 39.510 13.977 35.138 1.00 12.80 PROT ATOM 1402 CD1 PHE 403 40.545 12.957 34.693 1.00 5.42 PROT ATOM 1403 CD2 PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1404 CE1 PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1407 C PHE 403 39.080 13.366 37.539 1.00 10.08		ATOM	1381 CD1 LEU 400	41.616 20.594 33.195 1.00 2.00	PROT
ATOM 1384 O LEU 400 39.189 17.228 36.787 1.00 26.46 PROT ATOM 1385 N LEU 401 37.371 18.447 36.354 1.00 21.93 PROT ATOM 1386 CA LEU 401 36.862 18.268 37.707 1.00 17.21 PROT ATOM 1387 CB LEU 401 35.766 19.285 38.022 1.00 19.27 PROT ATOM 1389 CD1 LEU 401 36.652 20.403 40.085 1.00 2.00 PROT ATOM 1390 CD2 LEU 401 36.316 16.864 37.879 1.00 18.03 PROT ATOM 1392 O LEU 401 36.482 16.250 38.925 1.00 28.63 PROT ATOM 1393 N ALA 402 35.656 16.346 36.856 1.00 9.30 PROT ATOM 1394 CA ALA 402 35.124 15.000 36.951 1.00 7.03 PROT ATOM 1396 C ALA 402 36.298 14.029 36.989 1.00 7.68 PROT ATOM 1398 N PHE 403 36.298 14.029 36.989 1.00 7.68 PROT ATOM 1399 CA PHE 403 39.510 13.977 35.138 1.00 12.80 PROT ATOM 1400 CB PHE 403 39.510 13.977 35.138 1.00 12.80 PROT ATOM 1402 CD1 PHE 403 40.545 12.957 34.693 1.00 2.00 PROT ATOM 1404 CE1 PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1404 CE2 PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1407 C PHE 403 39.080 13.366 37.539 1.00 10.08		ATOM	1382 CD2 LEU 400	42.055 18.333 34.095 1.00 13.73	PROT
25 ATOM 1385 N LEU 401 37.371 18.447 36.354 1.00 21.93 PROT ATOM 1386 CA LEU 401 36.862 18.268 37.707 1.00 17.21 PROT ATOM 1387 CB LEU 401 35.766 19.285 38.022 1.00 19.27 PROT ATOM 1389 CD1 LEU 401 36.652 20.403 40.085 1.00 2.00 PROT ATOM 1390 CD2 LEU 401 36.316 16.864 37.879 1.00 14.41 PROT ATOM 1391 C LEU 401 36.482 16.250 38.925 1.00 28.63 PROT ATOM 1393 N ALA 402 35.656 16.346 36.856 1.00 9.30 PROT ATOM 1394 CA ALA 402 35.124 15.000 36.951 1.00 7.03 PROT ATOM 1395 CB ALA 402 35.224 15.000 36.951 1.00 7.03 PROT ATOM 1396 C ALA 402 36.298 14.029 36.989 1.00 7.68 PROT ATOM 1398 N PHE 403 36.298 14.029 36.989 1.00 7.68 PROT ATOM 1399 CA PHE 403 39.510 13.977 35.138 1.00 12.80 PROT ATOM 1400 CB PHE 403 40.545 12.957 34.693 1.00 5.42 PROT ATOM 1402 CD1 PHE 403 40.545 12.957 34.693 1.00 2.00 PROT ATOM 1404 CE1 PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1404 CE2 PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1407 C PHE 403 39.080 13.366 37.539 1.00 10.08		ATOM	1383 C LEU 400	38.527 17.892 36.002 1.00 24.79	PROT
ATOM 1386 CA LEU 401 36.862 18.268 37.707 1.00 17.21 PROT ATOM 1387 CB LEU 401 35.766 19.285 38.022 1.00 19.27 PROT ATOM 1388 CG LEU 401 36.553 19.547 39.515 1.00 16.76 PROT ATOM 1389 CD1 LEU 401 36.652 20.403 40.085 1.00 2.00 PROT ATOM 1390 CD2 LEU 401 36.316 16.864 37.879 1.00 18.03 PROT ATOM 1392 O LEU 401 36.482 16.250 38.925 1.00 28.63 PROT ATOM 1393 N ALA 402 35.656 16.346 36.856 1.00 9.30 PROT ATOM 1395 CB ALA 402 35.656 16.346 36.856 1.00 9.30 PROT ATOM 1396 C ALA 402 36.298 14.029 36.989 1.00 7.03 PROT ATOM 1397 O ALA 402 36.298 14.029 36.989 1.00 7.68 PROT ATOM 1398 N PHE 403 37.311 14.305 36.178 1.00 4.49 PROT ATOM 1399 CA PHE 403 39.510 13.977 35.138 1.00 12.80 PROT ATOM 1400 CB PHE 403 39.510 13.977 35.138 1.00 12.80 PROT ATOM 1402 CD1 PHE 403 40.545 12.957 34.693 1.00 5.42 PROT ATOM 1404 CE1 PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1404 CE2 PHE 403 42.546 12.410 33.4688 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1407 C PHE 403 39.080 13.366 37.539 1.00 10.08 PROT PROT ATOM 1407 C PHE 403 39.080 13.366 37.539 1.00 10.08		ATOM	1384 O LEU 400	39.189 17.228 36.787 1.00 26.46	PROT
ATOM 1387 CB LEU 401 35.766 19.285 38.022 1.00 19.27 PROT ATOM 1388 CG LEU 401 35.538 19.547 39.515 1.00 16.76 PROT ATOM 1389 CD1 LEU 401 36.652 20.403 40.085 1.00 2.00 PROT ATOM 1391 C LEU 401 36.316 16.864 37.879 1.00 18.03 PROT ATOM 1392 O LEU 401 36.482 16.250 38.925 1.00 28.63 PROT ATOM 1394 CA ALA 402 35.656 16.346 36.856 1.00 9.30 PROT ATOM 1395 CB ALA 402 35.124 15.000 36.951 1.00 7.03 PROT ATOM 1396 C ALA 402 36.298 14.029 36.989 1.00 7.68 PROT ATOM 1398 N PHE 403 37.311 14.305 36.178 1.00 4.49 PROT ATOM 1399 CA PHE 403 39.510 13.977 35.138 1.00 12.80 PROT ATOM 1400 CB PHE 403 39.510 13.977 35.138 1.00 12.80 PROT ATOM 1401 CG PHE 403 40.545 12.957 34.693 1.00 2.00 PROT ATOM 1403 CD2 PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1404 CE1 PHE 403 42.546 12.410 33.448 1.00 2.00 PROT ATOM 1405 CE2 PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1407 C PHE 403 39.080 13.366 37.539 1.00 10.08 PROT PROT ATOM 1407 C PHE 403 39.080 13.366 37.539 1.00 10.08	25	ATOM	1385 N LEU 401	37.371 18.447 36.354 1.00 21.93	PROT
ATOM 1387 CB LEU 401 35.766 19.285 38.022 1.00 19.27 PROT ATOM 1388 CG LEU 401 35.538 19.547 39.515 1.00 16.76 PROT ATOM 1389 CD1 LEU 401 36.652 20.403 40.085 1.00 2.00 PROT ATOM 1391 C LEU 401 36.316 16.864 37.879 1.00 18.03 PROT ATOM 1393 N ALA 402 35.656 16.346 36.856 1.00 9.30 PROT ATOM 1395 CB ALA 402 35.124 15.000 36.951 1.00 7.03 PROT ATOM 1397 O ALA 402 36.298 14.029 36.989 1.00 7.68 PROT ATOM 1398 N PHE 403 37.311 14.305 36.178 1.00 4.49 PROT ATOM 1399 CA PHE 403 39.510 13.977 35.138 1.00 12.80 PROT ATOM 1400 CB PHE 403 39.510 13.977 35.138 1.00 12.80 PROT ATOM 1401 CG PHE 403 40.545 12.957 34.693 1.00 2.00 PROT ATOM 1403 CD2 PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1404 CE1 PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1404 CE1 PHE 403 42.546 12.410 33.448 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1407 C PHE 403 39.080 13.366 37.539 1.00 10.08					PROT
ATOM 1389 CD1 LEU 401 36.652 20.403 40.085 1.00 2.00 PROT ATOM 1390 CD2 LEU 401 34.206 20.235 39.687 1.00 14.41 PROT ATOM 1391 C LEU 401 36.316 16.864 37.879 1.00 18.03 PROT ATOM 1392 O LEU 401 36.482 16.250 38.925 1.00 28.63 PROT ATOM 1393 N ALA 402 35.656 16.346 36.856 1.00 9.30 PROT ATOM 1394 CA ALA 402 35.124 15.000 36.951 1.00 7.03 PROT ATOM 1395 CB ALA 402 36.298 14.029 36.989 1.00 7.68 PROT ATOM 1397 O ALA 402 36.298 14.029 36.989 1.00 7.68 PROT ATOM 1398 N PHE 403 37.311 14.305 36.178 1.00 4.49 PROT ATOM 1399 CA PHE 403 39.510 13.977 35.138 1.00 12.80 PROT ATOM 1400 CB PHE 403 40.545 12.957 34.693 1.00 5.42 PROT ATOM 1402 CD1 PHE 403 40.545 12.957 34.693 1.00 2.00 PROT ATOM 1403 CD2 PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1404 CE1 PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1405 CE2 PHE 403 42.546 12.410 33.448 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1407 C PHE 403 39.080 13.366 37.539 1.00 10.08 PROT		ATOM	1387 CB LEU 401	35.766 19.285 38.022 1.00 19.27	PROT
30       ATOM       1390       CD2 LEU       401       34.206       20.235       39.687       1.00 14.41       PROT         ATOM       1391       C LEU       401       36.316       16.864       37.879       1.00 18.03       PROT         ATOM       1392       O LEU       401       36.316       16.864       37.879       1.00 18.03       PROT         ATOM       1393       N       ALA       402       36.482       16.250       38.925       1.00 28.63       PROT         ATOM       1394       CA       ALA       402       35.656       16.346       36.856       1.00       9.30       PROT         ATOM       1395       CB       ALA       402       35.124       15.000       36.951       1.00       7.03       PROT         ATOM       1396       C       ALA       402       36.298       14.029       36.989       1.00       7.68       PROT         ATOM       1397       O       ALA       402       36.294       13.054       37.739       1.00       2.00       PROT         ATOM       1399       CA       PHE       403       39.510       13.977       35.138       1.00		ATOM	1388 CG LEU 401	35.538 19.547 39.515 1.00 16.76	PROT
ATOM 1391 C LEU 401 36.316 16.864 37.879 1.00 18.03 PROT ATOM 1392 O LEU 401 36.482 16.250 38.925 1.00 28.63 PROT ATOM 1393 N ALA 402 35.656 16.346 36.856 1.00 9.30 PROT ATOM 1394 CA ALA 402 35.124 15.000 36.951 1.00 7.03 PROT ATOM 1395 CB ALA 402 36.298 14.029 36.989 1.00 7.68 PROT ATOM 1397 O ALA 402 36.298 14.029 36.989 1.00 7.68 PROT ATOM 1398 N PHE 403 37.311 14.305 36.178 1.00 4.49 PROT ATOM 1399 CA PHE 403 39.510 13.977 35.138 1.00 12.80 PROT ATOM 1400 CB PHE 403 39.510 13.977 35.138 1.00 12.80 PROT ATOM 1401 CG PHE 403 40.545 12.957 34.693 1.00 5.42 PROT ATOM 1403 CD2 PHE 403 40.545 12.957 34.693 1.00 2.00 PROT ATOM 1404 CE1 PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1404 CE1 PHE 403 42.546 12.410 33.448 1.00 2.00 PROT ATOM 1405 CE2 PHE 403 42.546 12.410 33.448 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1407 C PHE 403 39.080 13.366 37.539 1.00 10.08 PROT		ATOM	1389 CD1 LEU 401	36.652 20.403 40.085 1.00 2.00	PROT
ATOM 1392 O LEU 401 36.482 16.250 38.925 1.00 28.63 PROT ATOM 1393 N ALA 402 35.656 16.346 36.856 1.00 9.30 PROT ATOM 1394 CA ALA 402 35.124 15.000 36.951 1.00 7.03 PROT ATOM 1395 CB ALA 402 34.233 14.703 35.758 1.00 14.15 PROT ATOM 1396 C ALA 402 36.298 14.029 36.989 1.00 7.68 PROT ATOM 1397 O ALA 402 36.298 14.029 36.989 1.00 7.68 PROT ATOM 1398 N PHE 403 37.311 14.305 36.178 1.00 4.49 PROT ATOM 1399 CA PHE 403 38.477 13.439 36.140 1.00 9.18 PROT ATOM 1400 CB PHE 403 39.510 13.977 35.138 1.00 12.80 PROT ATOM 1401 CG PHE 403 40.545 12.957 34.693 1.00 5.42 PROT ATOM 1402 CD1 PHE 403 41.590 13.334 33.859 1.00 2.00 PROT ATOM 1403 CD2 PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1404 CE1 PHE 403 42.546 12.410 33.448 1.00 2.00 PROT ATOM 1405 CE2 PHE 403 42.546 12.410 33.448 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1407 C PHE 403 39.080 13.366 37.539 1.00 10.08 PROT	30	ATOM	1390 CD2 LEU 401	34.206 20.235 39.687 1.00 14.41	PROT
ATOM 1393 N ALA 402 35.656 16.346 36.856 1.00 9.30 PROT ATOM 1394 CA ALA 402 35.124 15.000 36.951 1.00 7.03 PROT ATOM 1395 CB ALA 402 34.233 14.703 35.758 1.00 14.15 PROT ATOM 1396 C ALA 402 36.298 14.029 36.989 1.00 7.68 PROT ATOM 1397 O ALA 402 36.294 13.054 37.739 1.00 2.00 PROT ATOM 1398 N PHE 403 37.311 14.305 36.178 1.00 4.49 PROT ATOM 1399 CA PHE 403 38.477 13.439 36.140 1.00 9.18 PROT ATOM 1400 CB PHE 403 39.510 13.977 35.138 1.00 12.80 PROT ATOM 1401 CG PHE 403 40.545 12.957 34.693 1.00 5.42 PROT ATOM 1402 CD1 PHE 403 40.545 12.957 34.693 1.00 5.42 PROT ATOM 1403 CD2 PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1404 CE1 PHE 403 42.546 12.410 33.448 1.00 2.00 PROT ATOM 1405 CE2 PHE 403 41.440 10.711 34.688 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1407 C PHE 403 39.080 13.366 37.539 1.00 10.08 PROT		ATOM	1391 C LEU 401	36.316 16.864 37.879 1.00 18.03	PROT
ATOM 1394 CA ALA 402 35.124 15.000 36.951 1.00 7.03 PROT ATOM 1395 CB ALA 402 36.298 14.029 36.989 1.00 7.68 PROT ATOM 1397 O ALA 402 36.294 13.054 37.739 1.00 2.00 PROT ATOM 1399 CA PHE 403 39.510 13.977 35.138 1.00 12.80 PROT ATOM 1400 CB PHE 403 40.545 12.957 34.693 1.00 5.42 PROT ATOM 1402 CD1 PHE 403 40.545 12.957 34.693 1.00 5.42 PROT ATOM 1403 CD2 PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1404 CE1 PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1404 CE1 PHE 403 42.546 12.410 33.448 1.00 2.00 PROT ATOM 1405 CE2 PHE 403 41.440 10.711 34.688 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1406 CZ PHE 403 39.080 13.366 37.539 1.00 10.08 PROT ATOM 1407 C PHE 403 39.080 13.366 37.539 1.00 10.08		ATOM	1392 O LEU 401	36.482 16.250 38.925 1.00 28.63	PROT
35         ATOM         1395         CB         ALA         402         34.233         14.703         35.758         1.00         14.15         PROT           ATOM         1396         C         ALA         402         36.298         14.029         36.989         1.00         7.68         PROT           ATOM         1397         O         ALA         402         36.294         13.054         37.739         1.00         2.00         PROT           ATOM         1398         N         PHE         403         37.311         14.305         36.178         1.00         4.49         PROT           ATOM         1399         CA         PHE         403         38.477         13.439         36.140         1.00         9.18         PROT           40         ATOM         1400         CB         PHE         403         39.510         13.977         35.138         1.00         12.80         PROT           ATOM         1401         CG         PHE         403         40.545         12.957         34.693         1.00         5.42         PROT           ATOM         1403         CD2         PHE         403         40.480         11.634		ATOM	1393 N ALA 402	35.656 16.346 36.856 1.00 9.30	PROT
35       ATOM       1395       CB       ALA       402       34.233       14.703       35.758       1.00       14.15       PROT         ATOM       1396       C       ALA       402       36.298       14.029       36.989       1.00       7.68       PROT         ATOM       1397       O       ALA       402       36.294       13.054       37.739       1.00       2.00       PROT         ATOM       1398       N       PHE       403       37.311       14.305       36.178       1.00       4.49       PROT         ATOM       1399       CA       PHE       403       38.477       13.439       36.140       1.00       9.18       PROT         40       ATOM       1400       CB       PHE       403       39.510       13.977       35.138       1.00       12.80       PROT         ATOM       1401       CG       PHE       403       40.545       12.957       34.693       1.00       5.42       PROT         ATOM       1403       CD2       PHE       403       40.480       11.634       35.103       1.00       2.00       PROT         45       ATOM       1404		ATOM	1394 CA ALA 402	35.124 15.000 36.951 1.00 7.03	PROT
ATOM 1396 C ALA 402 36.298 14.029 36.989 1.00 7.68 PROT ATOM 1397 O ALA 402 36.294 13.054 37.739 1.00 2.00 PROT ATOM 1398 N PHE 403 37.311 14.305 36.178 1.00 4.49 PROT ATOM 1399 CA PHE 403 38.477 13.439 36.140 1.00 9.18 PROT ATOM 1400 CB PHE 403 39.510 13.977 35.138 1.00 12.80 PROT ATOM 1401 CG PHE 403 40.545 12.957 34.693 1.00 5.42 PROT ATOM 1402 CD1 PHE 403 41.590 13.334 33.859 1.00 2.00 PROT ATOM 1404 CE1 PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1404 CE1 PHE 403 42.546 12.410 33.448 1.00 2.00 PROT ATOM 1405 CE2 PHE 403 41.440 10.711 34.688 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1407 C PHE 403 39.080 13.366 37.539 1.00 10.08 PROT	35	ATOM	1395 CB ALA 402	34.233 14.703 35.758 1.00 14.15	PROT
ATOM 1398 N PHE 403 37.311 14.305 36.178 1.00 4.49 PROT ATOM 1399 CA PHE 403 38.477 13.439 36.140 1.00 9.18 PROT 40 ATOM 1400 CB PHE 403 39.510 13.977 35.138 1.00 12.80 PROT ATOM 1401 CG PHE 403 40.545 12.957 34.693 1.00 5.42 PROT ATOM 1402 CD1 PHE 403 41.590 13.334 33.859 1.00 2.00 PROT ATOM 1403 CD2 PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1404 CE1 PHE 403 42.546 12.410 33.448 1.00 2.00 PROT ATOM 1405 CE2 PHE 403 41.440 10.711 34.688 1.00 2.00 PROT ATOM 1406 CZ PHE 403 39.080 13.366 37.539 1.00 10.08 PROT		ATOM	1396 C ALA 402	36.298 14.029 36.989 1.00 7.68	PROT
ATOM 1398 N PHE 403 37.311 14.305 36.178 1.00 4.49 PROT ATOM 1399 CA PHE 403 38.477 13.439 36.140 1.00 9.18 PROT 40 ATOM 1400 CB PHE 403 39.510 13.977 35.138 1.00 12.80 PROT ATOM 1401 CG PHE 403 40.545 12.957 34.693 1.00 5.42 PROT ATOM 1402 CD1 PHE 403 41.590 13.334 33.859 1.00 2.00 PROT ATOM 1403 CD2 PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1404 CE1 PHE 403 42.546 12.410 33.448 1.00 2.00 PROT ATOM 1405 CE2 PHE 403 41.440 10.711 34.688 1.00 2.00 PROT ATOM 1406 CZ PHE 403 39.080 13.366 37.539 1.00 10.08 PROT		ATOM	1397 O ALA 402	36.294 13.054 37.739 1.00 2.00	PROT
ATOM 1399 CA PHE 403 38.477 13.439 36.140 1.00 9.18 PROT  40 ATOM 1400 CB PHE 403 39.510 13.977 35.138 1.00 12.80 PROT  ATOM 1401 CG PHE 403 40.545 12.957 34.693 1.00 5.42 PROT  ATOM 1402 CD1 PHE 403 41.590 13.334 33.859 1.00 2.00 PROT  ATOM 1403 CD2 PHE 403 40.480 11.634 35.103 1.00 2.00 PROT  ATOM 1404 CE1 PHE 403 42.546 12.410 33.448 1.00 2.00 PROT  ATOM 1405 CE2 PHE 403 41.440 10.711 34.688 1.00 2.00 PROT  ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT  ATOM 1407 C PHE 403 39.080 13.366 37.539 1.00 10.08 PROT		ATOM			PROT
40       ATOM       1400       CB       PHE       403       39.510       13.977       35.138       1.00       12.80       PROT         ATOM       1401       CG       PHE       403       40.545       12.957       34.693       1.00       5.42       PROT         ATOM       1402       CD1       PHE       403       41.590       13.334       33.859       1.00       2.00       PROT         ATOM       1403       CE1       PHE       403       42.546       12.410       33.448       1.00       2.00       PROT         ATOM       1405       CE2       PHE       403       42.468       11.100       33.863       1.00       2.00       PROT         ATOM       1406       CZ       PHE       403       39.080       13.366       37.539       1.00       10.08       PROT					PROT
ATOM 1401 CG PHE 403 40.545 12.957 34.693 1.00 5.42 PROT ATOM 1402 CD1 PHE 403 41.590 13.334 33.859 1.00 2.00 PROT ATOM 1403 CD2 PHE 403 40.480 11.634 35.103 1.00 2.00 PROT ATOM 1404 CE1 PHE 403 42.546 12.410 33.448 1.00 2.00 PROT ATOM 1405 CE2 PHE 403 41.440 10.711 34.688 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1407 C PHE 403 39.080 13.366 37.539 1.00 10.08 PROT	40	ATOM	1400 CB PHE 403	39.510 13.977 35.138 1.00 12.80	PROT
ATOM 1402 CD1 PHE 403					PROT
ATOM 1403 CD2 PHE 403		ATOM			PROT
ATOM 1404 CE1 PHE 403 42.546 12.410 33.448 1.00 2.00 PROT 45 ATOM 1405 CE2 PHE 403 41.440 10.711 34.688 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1407 C PHE 403 39.080 13.366 37.539 1.00 10.08 PROT		ATOM		40.480 11.634 35.103 1.00 2.00	PROT
45 ATOM 1405 CE2 PHE 403 41.440 10.711 34.688 1.00 2.00 PROT ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1407 C PHE 403 39.080 13.366 37.539 1.00 10.08 PROT					
ATOM 1406 CZ PHE 403 42.468 11.100 33.863 1.00 2.00 PROT ATOM 1407 C PHE 403 39.080 13.366 37.539 1.00 10.08 PROT	45				PROT
ATOM 1407 C PHE 403 39.080 13.366 37.539 1.00 10.08 PROT					
11 ON 1700 O THE 703 37.207 12.277 30.077 1.00 0.23 1 ROT		ATOM	1408 O PHE 403	39.207 12.279 38.097 1.00 8.23	PROT
ATOM 1409 N GLU 404 39.451 14.514 38.103 1.00 12.64 PROT					
50 ATOM 1410 CA GLU 404 40.030 14.546 39.448 1.00 19.23 PROT	50				

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40.227 15.989 39.942 1.00 19.80
                                                             PROT
    ATOM 1411 CB GLU 404
                               41.532 16.220 40.728 1.00 24.03
    ATOM 1412 CG GLU 404
                                                             PROT
                               41.474 17.429 41.655 1.00 29.60
                                                             PROT
    ATOM 1413 CD GLU 404
                               41.706 18.565 41.182 1.00 29.51
                                                             PROT
    ATOM 1414 OE1 GLU 404
                               41.197 17.247 42.861 1.00 30.42
                                                             PROT
    ATOM 1415 OE2 GLU 404
    ATOM 1416 C GLU 404
                              39.112 13.806 40.416 1.00 24.36
                                                            PROT
    ATOM 1417 O GLU 404
                              39.571 12.963 41.200 1.00 28.04
                                                            PROT
    ATOM 1418 N HIS 405
                             37.815 14.108 40.358 1.00 10.26
                                                           PROT
    ATOM 1419 CA HIS 405
                              36.870 13.446 41.240 1.00 7.78
                                                            PROT
                              35.473 14.023 41.054 1.00 3.47
                                                           PROT
    ATOM 1420 CB HIS 405
10
    ATOM 1421 CG HIS 405
                              35.312 15.393 41.630 1.00 15.49
                                                            PROT
                               36.223 16.260 42.134 1.00 17.97
                                                            PROT
    ATOM 1422 CD2 HIS 405
                              34.096 16.036 41.694 1.00 21.57
                                                             PROT
    ATOM 1423 ND1 HIS 405
                              34.265 17.242 42.210 1.00 27.50
                                                            PROT
    ATOM 1424 CE1 HIS 405
                               35.547 17.403 42.485 1.00 13.53
                                                            PROT
    ATOM 1425 NE2 HIS 405
15
                             36.856 11.936 41.005 1.00 14.88
                                                           PROT
    ATOM 1426 C HIS 405
                             36.641 11.155 41.935 1.00 22.11
                                                           PROT
     ATOM 1427 O HIS 405
                              37.091 11.512 39.767 1.00 16.52
                                                            PROT
     ATOM 1428 N TYR 406
     ATOM 1429 CA TYR 406
                               37.085 10.083 39.491 1.00 14.35
                                                            PROT
                               37.007 9.808 37.989 1.00 9.90
                                                            PROT
     ATOM 1430 CB TYR 406
20
                               36.840 8.346 37.657 1.00 2.00
                                                            PROT
     ATOM 1431 CG TYR 406
                               35.587 7.742 37.676 1.00 8.84
                                                            PROT
     ATOM 1432 CD1 TYR 406
                               35.433 6.382 37.386 1.00 8.78
     ATOM 1433 CE1 TYR 406
                                                            PROT
                               37.939 7.562 37.338 1.00 15.34
                                                            PROT
     ATOM 1434 CD2 TYR 406
                               37.801 6.204 37.044 1.00 13.48
                                                             PROT
25
     ATOM 1435 CE2 TYR 406
     ATOM 1436 CZ TYR 406
                               36.548 5.624 37.073 1.00 15.64
                                                            PROT
                              36.431 4.287 36.804 1.00 2.00
                                                            PROT
     ATOM 1437 OH TYR 406
                              38.340 9.466 40.071 1.00 9.54
                                                           PROT
     ATOM 1438 C TYR 406
     ATOM 1439 O TYR 406
                              38.328 8.328 40.525 1.00 14.29
                                                           PROT
                             39.430 10.217 40.058 1.00 6.56
                                                           PROT
     ATOM 1440 N ILE 407
30
                                                           PROT
     ATOM 1441 CA ILE 407
                             40.671 9.708 40.617 1.00 13.87
                                                            PROT
     ATOM 1442 CB ILE 407
                              41.808 10.728 40.474 1.00 11.28
                              42.902 10.413 41.461 1.00 6.25
                                                            PROT
     ATOM 1443 CG2 ILE 407
                              42.357 10.714 39.039 1.00 18.73
                                                            PROT
     ATOM 1444 CG1 ILE 407
                               41.863 9.579 38.169 1.00 13.14
                                                            PROT
     ATOM 1445 CD1 ILE 407
35
                             40.438 9.426 42.091 1.00 11.44
                                                           PROT
     ATOM 1446 C ILE 407
                             40.691 8.325 42.571 1.00 4.46
                                                          PROT
     ATOM 1447 O ILE 407
                              39.953 10.448 42.792 1.00 12.35
                                                            PROT
     ATOM 1448 N ASN 408
     ATOM 1449 CA ASN 408
                               39.642 10.363 44.213 1.00 2.00
                                                            PROT
                                                             PROT
     ATOM 1450 CB ASN 408
                               38.758 11.535 44.629 1.00 2.00
40
                               39.499 12.840 44.657 1.00 3.57
                                                             PROT
     ATOM 1451 CG ASN 408
     ATOM 1452 OD1 ASN 408
                               40.733 12.859 44.656 1.00 14.35
                                                             PROT
     ATOM 1453 ND2 ASN 408
                                38.758 13.949 44.689 1.00 2.00
                                                             PROT
                              38.868 9.078 44.432 1.00 6.49
                                                           PROT
     ATOM 1454 C ASN 408
     ATOM 1455 O ASN 408
                              39.282 8.187 45.178 1.00 10.45
                                                            PROT
45
                              37.731 8.987 43.766 1.00 2.00
                                                           PROT
     ATOM 1456 N TYR 409
                              36.900 7.816 43.893 1.00 9.20
                                                           PROT
     ATOM 1457 CA TYR 409
     ATOM 1458 CB TYR 409
                               35.879 7.783 42.760 1.00 11.66
                                                            PROT
     ATOM 1459 CG TYR 409 35.121 6.489 42.683 1.00 12.54
                                                             PROT
     ATOM 1460 CD1 TYR 409 33.984 6.281 43.456 1.00 29.23
                                                            PROT
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PROT
    ATOM 1461 CE1 TYR 409
                               33.285 5.077 43.403 1.00 25.45
                               35.547 5.465 41.850 1.00 24.96
                                                            PROT
    ATOM 1462 CD2 TYR 409
                               34.860 4.259 41.788 1.00 33.40
                                                            PROT
    ATOM 1463 CE2 TYR 409
                              33.733 4.074 42.567 1.00 24.27
                                                           PROT
    ATOM 1464 CZ TYR 409
    ATOM 1465 OH TYR 409
                               33.065 2.883 42.509 1.00 32.72
                                                            PROT
                              37.753 6.553 43.867 1.00 13.96
    ATOM 1466 C TYR 409
                                                           PROT
    ATOM 1467 O TYR 409
                              37.730 5.763 44.804 1.00 29.48
                                                           PROT
                              38.531 6.399 42.803 1.00 23.04
                                                           PROT
    ATOM 1468 N ARG 410
                                                            PROT
    ATOM 1469 CA ARG 410
                              39.377 5.230 42.588 1.00 22.09
                               39.982 5.327 41.190 1.00 13.24
                                                            PROT
    ATOM 1470 CB ARG 410
10
                               38.947 5.399 40.090 1.00 14.01
                                                            PROT
    ATOM 1471 CG ARG 410
                               38.934 4.111 39.275 1.00 16.49
                                                            PROT
    ATOM 1472 CD ARG 410
    ATOM 1473 NE ARG 410
                               40.227 3.848 38.651 1.00 9.77
                                                           PROT
                               40.617 2.651 38.239 1.00 11.38
    ATOM 1474 CZ ARG 410
                                                            PROT
                              41.806 2.493 37.685 1.00 14.94
    ATOM 1475 NH1 ARG 410
                                                            PROT
15
                               39.810 1.613 38.375 1.00 12.78
                                                            PROT
    ATOM 1476 NH2 ARG 410
                              40.486 4.914 43.604 1.00 24.49
    ATOM 1477 C ARG 410
                                                           PROT
                              40.860 3.753 43.780 1.00 12.85
                                                           PROT
    ATOM 1478 O ARG 410
                              41.023 5.931 44.262 1.00 24.16
    ATOM 1479 N LYS 411
                                                           PROT
                              42.085 5.706 45.235 1.00 27.14
                                                           PROT
20
    ATOM 1480 CA LYS 411
                              41.525 5.069 46.516 1.00 37.40
                                                           PROT
    ATOM 1481 CB LYS 411
                              40.317 5.779 47.103 1.00 35.00
    ATOM 1482 CG LYS 411
                                                           PROT
                              39,406 4.788 47.804 1.00 40.83
                                                            PROT
    ATOM 1483 CD LYS 411
                              38.414 5.496 48.725 1.00 58.04
                                                           PROT
    ATOM 1484 CE LYS 411
    ATOM 1485 NZ LYS 411
                              38.833 5.496 50.168 1.00 54.40
                                                           PROT
25
                             43.186 4.814 44.664 1.00 28.02
                                                           PROT
    ATOM 1486 C LYS 411
                              43.209 3.598 44.876 1.00 25.00
                                                           PROT
    ATOM 1487 O LYS 411
    ATOM 1488 N HIS 412
                             44.091 5.438 43.923 1.00 30.05
                                                          PROT
    ATOM 1489 CA HIS 412
                              45.223 4.738 43.332 1.00 26.70
                                                          PROT
                              45.756 5.491 42.104 1.00 29.28
                                                           PROT
    ATOM 1490 CB HIS 412
30
                              44.953 5.289 40.857 1.00 18.44
                                                           PROT
    ATOM 1491 CG HIS 412
                              43.783 5.836 40.451 1.00 19.98
    ATOM 1492 CD2 HIS 412
                                                           PROT
    ATOM 1493 ND1 HIS 412
                              45.366 4.465 39.833 1.00 16.33
                                                           PROT
                              44.486 4.513 38.850 1.00 24.80
                                                           PROT
    ATOM 1494 CE1 HIS 412
                              43.516 5.338 39.200 1.00 23.01
                                                           PROT
    ATOM 1495 NE2 HIS 412
35
                             46.281 4.788 44.406 1.00 20.73
                                                          PROT
    ATOM 1496 C HIS 412
                             46.335 5.740 45.171 1.00 24.69
    ATOM 1497 O HIS 412
                                                          PROT
                             47.138 3.784 44.461 1.00 28.17
                                                          PROT
    ATOM 1498 N HIS 413
                             48.183 3.788 45.465 1.00 28.09
                                                          PROT
    ATOM 1499 CA HIS 413
                              48.219 2.426 46.144 1.00 21.71
                                                           PROT
40
    ATOM 1500 CB HIS 413
                              46.906 2.053 46.759 1.00 44.26
                                                           PROT
    ATOM 1501 CG HIS 413
                                                           PROT
    ATOM 1502 CD2 HIS 413
                              46.140 0.941 46.632 1.00 43.48
                              46.214 2.902 47.600 1.00 40.00
                                                           PROT
    ATOM 1503 ND1 HIS 413
                              45.080 2.328 47.962 1.00 47.35
                                                           PROT
    ATOM 1504 CE1 HIS 413
    ATOM 1505 NE2 HIS 413
                              45.011 1.137 47.390 1.00 35.50
                                                          PROT
45
                             49.527 4.194 44.875 1.00 26.49
                                                          PROT
    ATOM 1506 C HIS 413
    ATOM 1507 O HIS 413
                             50.483 3.421 44.829 1.00 31.82
                                                          PROT
    ATOM 1508 N VAL 414
                             49.555 5.439 44.411 1.00 18.32
                                                          PROT
    ATOM 1509 CA VAL 414 50.726 6.069 43.820 1.00 22.60
                                                            PROT
    ATOM 1510 CB VAL 414 50.718 5.966 42.290 1.00 32.50
                                                            PROT
50
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51.636 7.026 41.694 1.00 33.83
                                                              PROT
    ATOM 1511 CG1 VAL 414
                                51.169 4.574 41.863 1.00 40.20
                                                             PROT
    ATOM 1512 CG2 VAL 414
                               50.630 7.529 44.225 1.00 17.96
                                                            PROT
    ATOM 1513 C VAL 414
                               49.708 8.236 43.829 1.00 30.33
                                                            PROT
    ATOM 1514 O VAL 414
                               51.586 7.969 45.028 1.00 32.51
                                                            PROT
    ATOM 1515 N THR 415
                               51.601 9.332 45.531 1.00 35.31
                                                             PROT
    ATOM 1516 CA THR 415
                               52.779 9.529 46.511 1.00 49.75
                                                             PROT
    ATOM 1517 CB THR 415
                                53.023 10.930 46.702 1.00 60.64
                                                             PROT
    ATOM 1518 OG1 THR 415
                                54.038 8.850 45.974 1.00 50.83
                                                             PROT
    ATOM 1519 CG2 THR 415
                              51.668 10.387 44.436 1.00 31.44
                                                             PROT
    ATOM 1520 C THR 415
10
                               52,423 10,251 43,475 1.00 22.01
                                                             PROT
    ATOM 1521 O THR 415
                              50.865 11.437 44.607 1.00 24.94
                                                            PROT
    ATOM 1522 N HIS 416
                               50.781 12.559 43.671 1.00 27.82
                                                             PROT
    ATOM 1523 CA HIS 416
                              52.163 13.164 43.440 1.00 32.98
                                                             PROT
    ATOM 1524 CB HIS 416
                               52,776 13,747 44,671 1.00 44,74
                                                             PROT
    ATOM 1525 CG HIS 416
15
                               53.982 13.539 45.251 1.00 44.91
                                                             PROT
    ATOM 1526 CD2 HIS 416
                               52.121 14.665 45.462 1.00 49.20
                                                             PROT
    ATOM 1527 ND1 HIS 416
                               52.899 15.000 46.477 1.00 53.14
                                                             PROT
    ATOM 1528 CE1 HIS 416
                               54.033 14.330 46.373 1.00 41.72
                                                             PROT
    ATOM 1529 NE2 HIS 416
                              50.176 12.172 42.328 1.00 29.13
                                                            PROT
20
    ATOM 1530 C HIS 416
                              50.612 12.660 41.286 1.00 37.24
                                                            PROT
    ATOM 1531 O HIS 416
                              49.163 11.311 42.350 1.00 18.38
                                                             PROT
    ATOM 1532 N PHE 417
                               48.528 10.867 41.115 1.00 16.08
                                                             PROT
    ATOM 1533 CA PHE 417
                               47.295 10.029 41.407 1.00 17.89
                                                             PROT
    ATOM 1534 CB PHE 417
    ATOM 1535 CG PHE 417
                               47.021 8.997 40.364 1.00 16.15
                                                             PROT
25
                                                             PROT
                                47.980 8.044 40.051 1.00 16.55
    ATOM 1536 CD1 PHE 417
                                45.806 8.971 39.696 1.00 15.49
                                                             PROT
    ATOM 1537 CD2 PHE 417
                                47.727 7.081 39.087 1.00 19.81
                                                             PROT
    ATOM 1538 CE1 PHE 417
                                45.544 8.008 38.731 1.00 9.76
                                                             PROT
    ATOM 1539 CE2 PHE 417
                               46.501 7.064 38.427 1.00 5.25
                                                             PROT
    ATOM 1540 CZ PHE 417
30
                              48.117 11.990 40.187 1.00 14.51
                                                             PROT
    ATOM 1541 C PHE 417
                               48.636 12.119 39.081 1.00 18.44
                                                             PROT
    ATOM 1542 O PHE 417
                              47.171 12.800 40.640 1.00 21.08
                                                             PROT
     ATOM 1543 N TRP 418
                                                             PROT
                               46.688 13.900 39.828 1.00 16.28
    ATOM 1544 CA TRP 418
                               45.796 14.832 40.659 1.00 15.19
                                                             PROT
    ATOM 1545 CB TRP 418
35
                               45.002 15.746 39.802 1.00 16.60
                                                              PROT
     ATOM 1546 CG TRP 418
                                44.165 15.369 38.710 1.00 21.85
                                                              PROT
     ATOM 1547 CD2 TRP 418
                                43.690 16.557 38.118 1.00 22.53
                                                              PROT
     ATOM 1548 CE2 TRP 418
                                                              PROT
     ATOM 1549 CE3 TRP 418
                                43.771 14.138 38.170 1.00 16.42
                                44.999 17.107 39.836 1.00 21.01
                                                              PROT
40
     ATOM 1550 CD1 TRP 418
                                                              PROT
                                44.215 17.606 38.826 1.00 24.02
     ATOM 1551 NEI TRP 418
                                                              PROT
                                42.838 16.555 37.010 1.00 24.64
     ATOM 1552 CZ2 TRP 418
                                                              PROT
                                42.925 14.135 37.069 1.00 28.80
     ATOM 1553 CZ3 TRP 418
     ATOM 1554 CH2 TRP 418
                                42.467 15.337 36.500 1.00 21.25
                                                              PROT
                                                             PROT
                              47.834 14.676 39.192 1.00 16.17
45
     ATOM 1555 C TRP 418
                                                             PROT
                               47.928 14.764 37.977 1.00 19.51
     ATOM 1556 O TRP 418
                               48.723 15.250 40.007 1.00 19.59
                                                             PROT
     ATOM 1557 N PRO 419
                               48.757 15.274 41.477 1.00 19.81
                                                              PROT
     ATOM 1558 CD PRO 419
                              49.837 16.002 39.429 1.00 17.87
                                                              PROT
     ATOM 1559 CA PRO 419
                               50.720 16.309 40.629 1.00 6.85
                                                             PROT
     ATOM 1560 CB PRO 419
50
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49.785 16.326 41.764 1.00 25.11
                                                             PROT
    ATOM 1561 CG PRO 419
    ATOM 1562 C PRO 419
                              50.578 15.202 38.373 1.00 15.44
                                                             PROT
                              50.922 15.720 37.315 1.00 24.75
                                                            PROT
    ATOM 1563 O PRO 419
                              50.811 13.932 38.664 1.00 15.10
                                                            PROT
    ATOM 1564 N LYS 420
    ATOM 1565 CA LYS 420
                               51.534 13.056 37.748 1.00 20.59
                                                             PROT
                               51.900 11.746 38.471 1.00 28.85
                                                             PROT
    ATOM 1566 CB LYS 420
                                                             PROT
                               52.955 11.906 39.577 1.00 30.61
    ATOM 1567 CG LYS 420
    ATOM 1568 CD LYS 420
                               52.907 10.759 40.580 1.00 24.41
                                                             PROT
                               54.275 10.493 41.224 1.00 31.94
                                                             PROT
    ATOM 1569 CE LYS 420
    ATOM 1570 NZ LYS 420
                               54.485 9.040 41.557 1.00 27.34
                                                             PROT
10
    ATOM 1571 C LYS 420
                              50.779 12.757 36.445 1.00 17.36
                                                            PROT
                              51.393 12.439 35.437 1.00 26.28
    ATOM 1572 O LYS 420
                                                             PROT
                              49.455 12.859 36.474 1.00 16.34
                                                             PROT
    ATOM 1573 N LEU 421
                               48.627 12.614 35.297 1.00 9.38
                                                             PROT
    ATOM 1574 CA LEU 421
                                                             PROT
                               47.231 12.139 35.707 1.00 13.22
    ATOM 1575 CB LEU 421
15
                               46.739 10.818 35.107 1.00 15.75
    ATOM 1576 CG LEU 421
                                                             PROT
                                                             PROT
                                47.919 9.993 34.652 1.00 29.24
    ATOM 1577 CD1 LEU 421
    ATOM 1578 CD2 LEU 421
                                45.949 10.049 36.135 1.00 12.19
                                                              PROT
                              48.511 13.866 34.441 1.00 12.61
                                                             PROT
    ATOM 1579 C LEU 421
                              48.458 13.777 33.223 1.00 17.85
                                                             PROT
    ATOM 1580 O LEU 421
20
    ATOM 1581 N LEU 422
                               48.451 15.036 35.063 1.00 8.47
                                                            PROT
                               48.393 16.254 34.277 1.00 7.21
                                                             PROT
     ATOM 1582 CA LEU 422
                               48.160 17.468 35.164 1.00 2.00
                                                             PROT
     ATOM 1583 CB LEU 422
     ATOM 1584 CG LEU 422
                               46.941 17.445 36.088 1.00 12.16
                                                             PROT
    ATOM 1585 CD1 LEU 422
                                47.024 18.660 36.982 1.00 6.96
                                                             PROT
25
                                                             PROT
                                45.632 17.450 35.313 1.00 2.00
     ATOM 1586 CD2 LEU 422
                               49.748 16.365 33.567 1.00 10.59
                                                             PROT
     ATOM 1587 C LEU 422
                               49.851 16.938 32.477 1.00 13.48
                                                             PROT
     ATOM 1588 O LEU 422
                               50.786 15.804 34.185 1.00 2.29
                                                             PROT
     ATOM 1589 N MET 423
                                52.109 15.821 33.579 1.00 6.50
                                                             PROT
     ATOM 1590 CA MET 423
30
                                53.158 15.215 34.514 1.00 2.13
                                                             PROT
     ATOM 1591 CB MET 423
                                                              PROT
                                53.361 15.968 35.803 1.00 16.33
     ATOM 1592 CG MET 423
                                                              PROT
     ATOM 1593 SD MET 423
                                55.075 16.415 36.070 1.00 26.66
                                                              PROT
     ATOM 1594 CE MET 423
                                55.751 14.880 36.623 1.00 20.24
                               52.016 14.966 32.318 1.00 12.20
                                                             PROT
35
     ATOM 1595 C MET 423
     ATOM 1596 O MET 423
                               52.741 15.183 31.345 1.00 18.67
                                                             PROT
                               51.114 13.988 32.352 1.00 7.89
                                                            PROT
     ATOM 1597 N LYS 424
                               50.907 13.084 31.230 1.00 12.91
                                                             PROT
     ATOM 1598 CA LYS 424
                                                             PROT
                               49.990 11.924 31.645 1.00 5.14
     ATOM 1599 CB LYS 424
                               50.669 10.579 31.980 1.00 11.76
                                                              PROT
     ATOM 1600 CG LYS 424
40
                                52.187 10.590 31.866 1.00 3.70
                                                             PROT
     ATOM 1601 CD LYS 424
                                                             PROT
     ATOM 1602 CE LYS 424
                               52.844 10.020 33.113 1.00 7.84
                               54.335 9.959 32.995 1.00 25.86
                                                             PROT
     ATOM 1603 NZ LYS 424
                               50.293 13.840 30.046 1.00 17.44
                                                             PROT
     ATOM 1604 C LYS 424
                               50.650 13.596 28.897 1.00 11.72
                                                             PROT
     ATOM 1605 O LYS 424
45
     ATOM 1606 N VAL 425
                               49.370 14.756 30.322 1.00 3.16
                                                             PROT
     ATOM 1607 CA VAL 425
                               48.768 15.515 29.249 1.00 2.00
                                                             PROT
                                47.744 16.532 29.773 1.00 6.77
                                                             PROT
     ATOM 1608 CB VAL 425
     ATOM 1609 CG1 VAL 425 47.653 17.716 28.815 1.00 2.00
                                                              PROT
                                46.381 15.870 29.914 1.00 10.91
     ATOM 1610 CG2 VAL 425
                                                             PROT
50
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PROT
                               49.845 16.274 28.487 1.00 4.83
     ATOM 1611 C VAL 425
                               49.853 16.265 27.269 1.00 15.69
    ATOM 1612 O VAL 425
                                                             PROT
    ATOM 1613 N THR 426
                               50.753 16.924 29.208 1.00 14.38
                                                             PROT
                               51.824 17.707 28.593 1.00 12.41
                                                              PROT
    ATOM 1614 CA THR 426
                               52.713 18.372 29.667 1.00 12.49
                                                              PROT
     ATOM 1615 CB THR 426
    ATOM 1616 OG1 THR 426
                                51.890 19.138 30.552 1.00 11.06
                                                              PROT
    ATOM 1617 CG2 THR 426
                                53.763 19.283 29.015 1.00 2.93
                                                              PROT
                               52.734 16.928 27.653 1.00 15.72
                                                             PROT
    ATOM 1618 C THR 426
    ATOM 1619 O THR 426
                               53.198 17.463 26.651 1.00 14.40
                                                             PROT
    ATOM 1620 N ASP 427
                              53.000 15.672 27.981 1.00 16.23
                                                             PROT
10
                               53.865 14.843 27.157 1.00 16.35
                                                             PROT
     ATOM 1621 CA ASP 427
                               54.342 13.630 27.950 1.00 19.48
                                                             PROT
     ATOM 1622 CB ASP 427
    ATOM 1623 CG ASP 427
                               55.337 13.997 29.029 1.00 18.96
                                                             PROT
                                55.874 15.125 29.010 1.00 8.75
                                                              PROT
    ATOM 1624 OD1 ASP 427
                                                              PROT
                                55.579 13.145 29.902 1.00 24.25
     ATOM 1625 OD2 ASP 427
15
                              53.155 14.381 25.891 1.00 20.52
                                                             PROT
     ATOM 1626 C ASP 427
                               53.793 14.164 24.856 1.00 25.69
                                                             PROT
     ATOM 1627 O ASP 427
                               51.838 14.218 25.986 1.00 5.49
                                                            PROT
    ATOM 1628 N LEU 428
     ATOM 1629 CA LEU 428
                               51.040 13.815 24.849 1.00 2.00
                                                             PROT
                               49.634 13.470 25.301 1.00 2.00
    ATOM 1630 CB LEU 428
                                                             PROT
20
     ATOM 1631 CG LEU 428
                               49.579 12.127 26.028 1.00 2.00
                                                             PROT
                                48.184 11.789 26.481 1.00 2.00
                                                              PROT
     ATOM 1632 CD1 LEU 428
                                50.088 11.080 25.108 1.00 2.00
     ATOM 1633 CD2 LEU 428
                                                              PROT
                               51.019 14.987 23.881 1.00 7.72
                                                            PROT
     ATOM 1634 C LEU 428
                               51.072 14.800 22.666 1.00 9.22
                                                             PROT
     ATOM 1635 O LEU 428
25
                               50.961 16.197 24.432 1.00 10.07
     ATOM 1636 N ARG 429
                                                             PROT
                                50.948 17.438 23.659 1.00 7.97
                                                             PROT
     ATOM 1637 CA ARG 429
                                50.799 18.642 24.583 1.00 18.55
                                                              PROT
     ATOM 1638 CB ARG 429
                                49.548 18.634 25.429 1.00 14.80
     ATOM 1639 CG ARG 429
                                                              PROT
                                48.588 19.674 24.935 1.00 32.08
                                                              PROT
     ATOM 1640 CD ARG 429
30
                                47.508 19.923 25.880 1.00 42.46
                                                              PROT
     ATOM 1641 NE ARG 429
                                46.226 19.673 25.631 1.00 48.51
                                                              PROT
     ATOM 1642 CZ ARG 429
                                45.860 19.163 24.459 1.00 33.35
                                                              PROT
     ATOM 1643 NH1 ARG 429
                                45.307 19.955 26.549 1.00 46.08
                                                              PROT
     ATOM 1644 NH2 ARG 429
     ATOM 1645 C ARG 429
                               52.260 17.557 22.919 1.00 11.77
                                                             PROT
35
     ATOM 1646 O ARG 429
                               52.298 17.904 21.737 1.00 28.66
                                                             PROT
                               53.343 17.270 23.629 1.00 20.26
                                                             PROT
     ATOM 1647 N MET 430
                                54.671 17.328 23.042 1.00 21.06
                                                              PROT
     ATOM 1648 CA MET 430
                                55.738 17.015 24.100 1.00 30.24
                                                              PROT
     ATOM 1649 CB MET 430
     ATOM 1650 CG MET 430
                                                              PROT
                                56.061 18.165 25.056 1.00 34.66
40
                                                              PROT
                                55.727 19.795 24.373 1.00 35.91
     ATOM 1651 SD MET 430
     ATOM 1652 CE MET 430
                                56.839 19.814 22.978 1.00 32.52
                                                              PROT
                               54.735 16.302 21.925 1.00 18.70
                                                             PROT
     ATOM 1653 C MET 430
                               55.287 16.560 20.860 1.00 16.59
                                                             PROT
     ATOM 1654 O MET 430
     ATOM 1655 N ILE 431
                              54.161 15.133 22.182 1.00 15.38
                                                            PROT
45
     ATOM 1656 CA ILE 431
                               54.144 14.069 21.196 1.00 15.85
                                                             PROT
                               53.326 12.859 21.705 1.00 13.76
     ATOM 1657 CB ILE 431
                                                             PROT
     ATOM 1658 CG2 ILE 431
                               52.727 12.084 20.539 1.00 11.11
                                                              PROT
                             54.239 11.924 22.489 1.00 11.72
                                                              PROT
     ATOM 1659 CG1 ILE 431
                               53.552 11.224 23.615 1.00 16.22
                                                              PROT
50
     ATOM 1660 CD1 ILE 431
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53.538 14.609 19.904 1.00 18.49
                                                            PROT
    ATOM 1661 C ILE 431
                              54.134 14.483 18.839 1.00 17.36
                                                            PROT
    ATOM 1662 O ILE 431
                               52.361 15.220 20.003 1.00 2.00
                                                            PROT
    ATOM 1663 N GLY 432
                                                             PROT
                               51.721 15.772 18.831 1.00 2.00
    ATOM 1664 CA GLY 432
                               52.542 16.851 18.148 1.00 10.55
                                                             PROT
    ATOM 1665 C GLY 432
    ATOM 1666 O GLY 432
                               52.707 16.834 16.936 1.00 9.60
                                                             PROT
                               53.043 17.805 18.926 1.00 11.17
                                                             PROT
    ATOM 1667 N ALA 433
                               53.855 18.884 18.385 1.00 2.00
    ATOM 1668 CA ALA 433
                                                             PROT
                               54.326 19.771 19.506 1.00 2.00
    ATOM 1669 CB ALA 433
                                                             PROT
                               55.050 18.285 17.646 1.00 6.43
                                                            PROT
    ATOM 1670 C ALA 433
10
                               55.493 18.789 16.623 1.00 11.71
                                                             PROT
    ATOM 1671 O ALA 433
                               55.579 17.197 18.179 1.00 15.71
                                                             PROT
    ATOM 1672 N CYS 434
                                                             PROT
    ATOM 1673 CA CYS 434
                               56.715 16.534 17.573 1.00 13.44
                               57.228 15.464 18.518 1.00 14.76
                                                             PROT
    ATOM 1674 CB CYS 434
                                                             PROT
                               58.910 15.703 18.985 1.00 20.82
    ATOM 1675 SG CYS 434
15
                               56.269 15.902 16.264 1.00 9.28
                                                            PROT
     ATOM 1676 C CYS 434
                               56.969 15.948 15.256 1.00 8.50
                                                            PROT
    ATOM 1677 O CYS 434
                              55.091 15.300 16.298 1.00 11.04
                                                            PROT
    ATOM 1678 N HIS 435
                               54.533 14.657 15.122 1.00 11.30
     ATOM 1679 CA HIS 435
                                                             PROT
                               53.142 14.132 15.438 1.00 4.30
                                                            PROT
20
     ATOM 1680 CB HIS 435
                                                             PROT
    ATOM 1681 CG HIS 435
                               52.480 13.460 14.283 1.00 13.68
                               52.751 12.288 13.662 1.00 4.72
                                                             PROT
     ATOM 1682 CD2 HIS 435
                               51.358 13.976 13.666 1.00 5.53
                                                             PROT
     ATOM 1683 ND1 HIS 435
                                                             PROT
                               50.966 13.147 12.717 1.00 12.84
     ATOM 1684 CE1 HIS 435
                                                             PROT
     ATOM 1685 NE2 HIS 435
                               51.794 12.116 12.694 1.00 15.77
25
                              54.482 15.661 13.973 1.00 8.50
                                                            PROT
     ATOM 1686 C HIS 435
                                                            PROT
                              54.941 15.370 12.869 1.00 14.82
     ATOM 1687 O HIS 435
                               53.938 16.844 14.245 1.00 5.74
                                                             PROT
     ATOM 1688 N ALA 436
                                53.843 17.905 13.252 1.00 2.00
                                                             PROT
     ATOM 1689 CA ALA 436
                                53.632 19.241 13.942 1.00 2.00
                                                             PROT
     ATOM 1690 CB ALA 436
30
                               55.121 17.934 12.406 1.00 8.68
                                                             PROT
     ATOM 1691 C ALA 436
                               55.080 17.712 11.193 1.00 15.14
                                                             PROT
     ATOM 1692 O ALA 436
                               56.256 18.189 13.047 1.00 6.82
                                                            PROT
     ATOM 1693 N SER 437
                               57.522 18.226 12.337 1.00 9.05
                                                             PROT
     ATOM 1694 CA SER 437
                               58.671 18.511 13.295 1.00 2.00
                                                             PROT
     ATOM 1695 CB SER 437
35
                                59.593 19.406 12.699 1.00 21.18
                                                             PROT
     ATOM 1696 OG SER 437
                                                             PROT
                               57.758 16.896 11.637 1.00 15.18
     ATOM 1697 C SER 437
                                                             PROT
                               58.076 16.849 10.445 1.00 19.33
     ATOM 1698 O SER 437
                               57.607 15.805 12.373 1.00 16.98
                                                             PROT
     ATOM 1699 N ARG 438
                                                              PROT
                                57,799 14,501 11,766 1.00 16.98
     ATOM 1700 CA ARG 438
40
                                                              PROT
                                57.294 13.409 12.702 1.00 24.77
     ATOM 1701 CB ARG 438
                                58.006 12.086 12.534 1.00 33.76
                                                              PROT
     ATOM 1702 CG ARG 438
                                59.506 12.280 12.614 1.00 30.64
                                                              PROT
     ATOM 1703 CD ARG 438
                                60.219 11.380 11.721 1.00 29.76
                                                              PROT
     ATOM 1704 NE ARG 438
                                61.505 11.504 11.423 1.00 25.21
                                                              PROT
     ATOM 1705 CZ ARG 438
45
                                 62.077 10.641 10.603 1.00 39.58
                                                               PROT
     ATOM 1706 NH1 ARG 438
                                 62.217 12.492 11.942 1.00 14.13
                                                               PROT
     ATOM 1707 NH2 ARG 438
                                                             PROT
                               57.031 14.441 10.448 1.00 16.49
     ATOM 1708 C ARG 438
                               57.563 14.008 9.424 1.00 15.57
                                                             PROT
     ATOM 1709 O ARG 438
                                                             PROT
                               55.781 14.893 10.484 1.00 16.75
     ATOM 1710 N PHE 439
50
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54.933 14.878 9.303 1.00 21.63
                                                            PROT
    ATOM 1711 CA PHE 439
    ATOM 1712 CB PHE 439
                               53.603 15.575 9.574 1.00 17.84
                                                            PROT
                               52.597 15.364 8.490 1.00 20.60
    ATOM 1713 CG PHE 439
                                                            PROT
                               52.042 14.103 8.279 1.00 30.60
                                                             PROT
    ATOM 1714 CD1 PHE 439
                               52.265 16.394 7.622 1.00 14.95
                                                             PROT
    ATOM 1715 CD2 PHE 439
                               51.175 13.867 7.206 1.00 29.12
    ATOM 1716 CE1 PHE 439
                                                             PROT
                               51.404 16.173 6.552 1.00 25.18
                                                             PROT
    ATOM 1717 CE2 PHE 439
                               50.860 14.905 6.341 1.00 27.82
    ATOM 1718 CZ PHE 439
                                                            PROT
    ATOM 1719 C PHE 439
                              55.620 15.548 8.130 1.00 28.17
                                                            PROT
    ATOM 1720 O PHE 439
                              55.512 15.095 6.987 1.00 28.83
                                                            PROT
10
    ATOM 1721 N LEU 440
                              56.328 16.633 8.427 1.00 26.77
                                                            PROT
                               57.055 17.382 7.418 1.00 24.66
                                                            PROT
    ATOM 1722 CA LEU 440
                               57.555 18.696 8.005 1.00 10.80
                                                            PROT
    ATOM 1723 CB LEU 440
    ATOM 1724 CG LEU 440
                               56.501 19.658 8.541 1.00 8.60
                                                            PROT
                               57.152 20.985 8.855 1.00 17.69
                                                            PROT
    ATOM 1725 CD1 LEU 440
15
    ATOM 1726 CD2 LEU 440
                                55.410 19.847 7.522 1.00 15.71
                                                             PROT
                              58.245 16.578 6.912 1.00 29.61
                                                            PROT
    ATOM 1727 C LEU 440
                              58.506 16.526 5.718 1.00 32.37
                                                            PROT
    ATOM 1728 O LEU 440
    ATOM 1729 N HIS 441
                              58.971 15.954 7.830 1.00 28.12
                                                           PROT
    ATOM 1730 CA HIS 441
                              60.140 15.172 7.460 1.00 28.51
                                                           PROT
20
                              60.783 14.564 8.705 1.00 36.77
                                                            PROT
    ATOM 1731 CB HIS 441
                              59.724 14.081 6.497 1.00 31.94
                                                           PROT
    ATOM 1732 C HIS 441
    ATOM 1733 O HIS 441
                             60.461 13.725 5.579 1.00 49.29
                                                           PROT
                               58.533 13.545 6.711 1.00 41.16
                                                            PROT
    ATOM 1734 N MET 442
                               58.033 12.487 5.854 1.00 39.99
                                                            PROT
25
    ATOM 1735 CA MET 442
                               56.871 11.776 6.551 1.00 38.32
    ATOM 1736 CB MET 442
                                                             PROT
                               57.263 11.122 7.860 1.00 19.20
                                                             PROT
    ATOM 1737 CG MET 442
                               55.859 10.350 8.675 1.00 38.06
                                                             PROT
    ATOM 1738 SD MET 442
    ATOM 1739 CE MET 442
                               54.906 11.767 9.073 1.00 21.45
                                                             PROT
                               57.599 13.031 4.495 1.00 35.68
                                                            PROT
    ATOM 1740 C MET 442
30
                               57.887 12.431 3.461 1.00 27.43
                                                            PROT
    ATOM 1741 O MET 442
                              56.920 14.175 4.503 1.00 34.17
    ATOM 1742 N LYS 443
                                                            PROT
                               56.447 14.796 3.268 1.00 34.33
                                                            PROT
    ATOM 1743 CA LYS 443
    ATOM 1744 CB LYS 443
                               55.767 16.129 3.574 1.00 21.68
                                                            PROT
                               54.303 15.989 3.953 1.00 26.95
                                                            PROT
    ATOM 1745 CG LYS 443
35
                               53.497 17.231 3.602 1.00 30.78
                                                            PROT
    ATOM 1746 CD LYS 443
                               52.204 16.848 2.861 1.00 56.06
                                                            PROT
    ATOM 1747 CE LYS 443
                               50.931 17.261 3.564 1.00 45.26
                                                            PROT
    ATOM 1748 NZ LYS 443
                              57.570 15.007 2.251 1.00 37.81
    ATOM 1749 C LYS 443
                                                            PROT
                              57.325 15.049 1.041 1.00 38.26
                                                            PROT
    ATOM 1750 O LYS 443
40
     ATOM 1751 N VAL 444
                               58.798 15.130 2.741 1.00 25.12
                                                            PROT
    ATOM 1752 CA VAL 444
                               59.942 15.318 1.867 1.00 25.43
                                                             PROT
                               60.802 16.531 2.334 1.00 29.15
    ATOM 1753 CB VAL 444
                                                             PROT
                                                             PROT
    ATOM 1754 CG1 VAL 444
                                59.893 17.621 2.861 1.00 29.48
    ATOM 1755 CG2 VAL 444
                                61.785 16.121 3.419 1.00 36.65
                                                             PROT
45
                               60.786 14.042 1.825 1.00 30.03
                                                            PROT
     ATOM 1756 C VAL 444
                               62.009 14.099 1.698 1.00 39.43
                                                            PROT
     ATOM 1757 O VAL 444
     ATOM 1758 N GLU 445
                               60.127 12.888 1.903 1.00 39.84
                                                            PROT
                              60.842 11.612 1.896 1.00 43.07
                                                             PROT
    ATOM 1759 CA GLU 445
    ATOM 1760 CB GLU 445
                              61.429 11.360 3.282 1.00 50.55
                                                             PROT
50
```

```
62.399 10.203 3.351 1.00 77.00
                                                             PROT
    ATOM 1761 CG GLU 445
    ATOM 1762 CD GLU 445
                               63.569 10.495 4.267 1.00 98.21
                                                             PROT
                               64.251 9.538 4.701 1.00100.00
    ATOM 1763 OE1 GLU 445
                                                             PROT
                               63.804 11.690 4.554 1.00100.00
                                                            PROT
    ATOM 1764 OE2 GLU 445
    ATOM 1765 C GLU 445
                              59.989 10.408 1.491 1.00 43.41
                                                            PROT
    ATOM 1766 O GLU 445
                              60.466 9.274 1.511 1.00 48.80
                                                           PROT
                              58.731 10.644 1.137 1.00 38.17
                                                            PROT
    ATOM 1767 N CYS 446
    ATOM 1768 CA CYS 446
                               57.852 9.548 0.743 1.00 41.38
                                                            PROT
    ATOM 1769 CB CYS 446
                               57.066 9.035 1.965 1.00 40.61
                                                            PROT
    ATOM 1770 SG CYS 446
                               58.062 8.276 3.320 1.00 44.73
                                                            PROT
10
                              56.886 10.003 -0.362 1.00 45.83
    ATOM 1771 C CYS 446
                                                            PROT
    ATOM 1772 O CYS 446
                              56.466 11.184 -0.323 1.00 44.17
                                                            PROT
                               56.570 9.180 -1.259 1.00 40.79
    ATOM 1773 OT CYS 446
                                                            PROT
    ATOM 1774 CB GLU 449
                               52.635 12.140 -2.649 1.00 28.60
                                                            PROT
                              52.019 10.014 -1.526 1.00 38.06
15
    ATOM 1775 C GLU 449
                                                            PROT
    ATOM 1776 O GLU 449
                              50.873 10.220 -1.935 1.00 43.52
                                                            PROT
    ATOM 1777 N GLU 449
                              54.378 10.460 -2.167 1.00 17.78
                                                            PROT
                              53.105 11.069 -1.689 1.00 33.80
    ATOM 1778 CA GLU 449
                                                           PROT
                              52.387 8.880 -0.936 1.00 46.88
    ATOM 1779 N LEU 450
                                                           PROT
                               51.432 7.808 -0.696 1.00 52.62
20
    ATOM 1780 CA LEU 450
                                                            PROT
    ATOM 1781 CB LEU 450
                               52.101 6.436 -0.850 1.00 57.50
                                                            PROT
                               53.338 6.066 -0.028 1.00 59.81
    ATOM 1782 CG LEU 450
                                                            PROT
    ATOM 1783 CD1 LEU 450
                               53.613 4.573 -0.198 1.00 51.33
                                                            PROT
                               54.544 6.890 -0.473 1.00 57.03
                                                            PROT
    ATOM 1784 CD2 LEU 450
25
    ATOM 1785 C LEU 450
                              50.850 7.970 0.711 1.00 50.65
                                                           PROT
    ATOM 1786 O LEU 450
                              50.965 7.091 1.569 1.00 38.49
                                                           PROT
                              50.225 9.123 0.923 1.00 32.24
                                                           PROT
    ATOM 1787 N PHE 451
                               49.602 9.478 2.188 1.00 32.64
    ATOM 1788 CA PHE 451
                                                            PROT
                               50.091 10.857 2.648 1.00 56.06
    ATOM 1789 CB PHE 451
                                                            PROT
                               51.534 10.895 3.056 1.00 61.73
    ATOM 1790 CG PHE 451
                                                            PROT
30
    ATOM 1791 CD1 PHE 451
                               52.523 10.366 2.235 1.00 66.92
                                                             PROT
                               51.905 11.486 4.256 1.00 58.76
    ATOM 1792 CD2 PHE 451
                                                             PROT
    ATOM 1793 CE1 PHE 451
                               53.860 10.430 2.604 1.00 69.17
                                                             PROT
                               53.231 11.556 4.635 1.00 61.48
                                                            PROT
    ATOM 1794 CE2 PHE 451
                               54.214 11.028 3.809 1.00 71.95
                                                            PROT
35
    ATOM 1795 CZ PHE 451
    ATOM 1796 C PHE 451
                              48.081 9.548 2.025 1.00 30.67
                                                           PROT
                              47.571 10.429 1.324 1.00 38.49
    ATOM 1797 O PHE 451
                                                           PROT
                              47.336 8.627 2.672 1.00 19.14
                                                           PROT
    ATOM 1798 N PRO 452
    ATOM 1799 CD PRO 452
                               47.774 7.495 3.510 1.00 24.21
                                                            PROT
                               45.881 8.672 2.538 1.00 5.88
    ATOM 1800 CA PRO 452
                                                            PROT
40
    ATOM 1801 CB PRO 452
                               45.397 7.742 3.633 1.00 16.92
                                                            PROT
     ATOM 1802 CG PRO 452
                               46.496 6.737 3.761 1.00 16.91
                                                            PROT
    ATOM 1803 C PRO 452
                              45.354 10.090 2.687 1.00 15.15
                                                            PROT
    ATOM 1804 O PRO 452
                              45.879 10.886 3.463 1.00 22.59
                                                            PROT
     ATOM 1805 N PRO 453
                              44.315 10.429 1.920 1.00 18.37
                                                            PROT
45
                               43.653 9.540 0.951 1.00 3.83
     ATOM 1806 CD PRO 453
                                                            PROT
                               43.710 11.766 1.960 1.00 14.00
     ATOM 1807 CA PRO 453
                                                            PROT
     ATOM 1808 CB PRO 453
                               42.502 11.649 1.032 1.00 20.04
                                                            PROT
                               42.316 10.163 0.807 1.00 19.43
                                                            PROT
    ATOM 1809 CG PRO 453
                              43.321 12.277 3.346 1.00 14.70
                                                            PROT
50
    ATOM 1810 C PRO 453
```

```
43.609 13.422 3.682 1.00 9.70
                                                          PROT
    ATOM 1811 O PRO 453
                             42.667 11.446 4.152 1.00 25.39
                                                          PROT
    ATOM 1812 N LEU 454
                              42.261 11.886 5.491 1.00 28.61
                                                           PROT
    ATOM 1813 CA LEU 454
                              41.463 10.804 6.217 1.00 17.29
                                                           PROT
    ATOM 1814 CB LEU 454
                              40.893 11.224 7.572 1.00 9.05
                                                           PROT
    ATOM 1815 CG LEU 454
    ATOM 1816 CD1 LEU 454
                              40.174 12.547 7.435 1.00 17.23
                                                           PROT
                               39.946 10.148 8.079 1.00 8.05
                                                           PROT
    ATOM 1817 CD2 LEU 454
                             43.479 12.234 6.316 1.00 23.36
                                                          PROT
    ATOM 1818 C LEU 454
                             43.484 13.225 7.037 1.00 10.99
    ATOM 1819 O LEU 454
                                                          PROT
                             44.503 11.394 6.205 1.00 14.26
                                                          PROT
    ATOM 1820 N PHE 455
10
    ATOM 1821 CA PHE 455
                              45,769 11.595 6.902 1.00 15.33
                                                           PROT
                              46.761 10.496 6.501 1.00 26.32
                                                           PROT
    ATOM 1822 CB PHE 455
                              48.138 10.644 7.108 1.00 43.03
                                                           PROT
    ATOM 1823 CG PHE 455
                              48.305 11.094 8.414 1.00 43.52
    ATOM 1824 CD1 PHE 455
                                                           PROT
                               49.270 10.282 6.380 1.00 41.44
                                                           PROT
    ATOM 1825 CD2 PHE 455
15
                              49.576 11.176 8.987 1.00 37.77
                                                           PROT
    ATOM 1826 CE1 PHE 455
                              50.536 10.363 6.947 1.00 49.43
                                                           PROT
    ATOM 1827 CE2 PHE 455
                              50.686 10.811 8.255 1.00 39.99
                                                           PROT
    ATOM 1828 CZ PHE 455
                             46.313 12.956 6.500 1.00 19.37
    ATOM 1829 C PHE 455
                                                          PROT
                             46.945 13.646 7.298 1.00 29.31
    ATOM 1830 O PHE 455
                                                          PROT
20
                             46.048 13.345 5.257 1.00 17.16
                                                          PROT
    ATOM 1831 N LEU 456
    ATOM 1832 CA LEU 456 46.527 14.625 4.750 1.00 20.15
                                                           PROT
                              46.572 14.603 3.218 1.00 35.14
                                                           PROT
    ATOM 1833 CB LEU 456
                              47.593 13.660 2.568 1.00 40.45
                                                           PROT
    ATOM 1834 CG LEU 456
                             47.233 13.456 1.116 1.00 44.38
                                                            PROT
25
    ATOM 1835 CD1 LEU 456
                              48.990 14.234 2.680 1.00 34.88
    ATOM 1836 CD2 LEU 456
                                                           PROT
                             45.680 15.800 5.226 1.00 20.37
                                                          PROT
    ATOM 1837 C LEU 456
                              46.207 16.866 5.548 1.00 29.61
                                                          PROT
    ATOM 1838 O LEU 456
    ATOM 1839 N GLU 457
                              44.367 15.607 5.280 1.00 13.06
                                                           PROT
                              43.483 16.675 5.713 1.00 14.14
                                                           PROT
    ATOM 1840 CA GLU 457
30
                              42.037 16.256 5.516 1.00 29.57
                                                           PROT
    ATOM 1841 CB GLU 457
                              43.731 17.058 7.173 1.00 14.95
                                                           PROT
    ATOM 1842 C GLU 457
                              43.771 18.237 7.514 1.00 15.98
                                                           PROT
    ATOM 1843 O GLU 457
                              43.901 16.051 8.026 1.00 26.34
    ATOM 1844 N VAL 458
                                                           PROT
                             44.143 16.260 9.455 1.00 24.39
                                                           PROT
    ATOM 1845 CA VAL 458
35
                              44.219 14.910 10.208 1.00 20.14
                                                            PROT
    ATOM 1846 CB VAL 458
    ATOM 1847 CG1 VAL 458
                              44.882 15.102 11.554 1.00 22.01
                                                           PROT
                               42.831 14.341 10.400 1.00 28.11
                                                            PROT
    ATOM 1848 CG2 VAL 458
    ATOM 1849 C VAL 458
                              45.417 17.039 9.778 1.00 21.50
                                                           PROT
    ATOM 1850 O VAL 458
                                                           PROT
                              45.364 18.062 10.439 1.00 18.85
40
    ATOM 1851 N PHE 459
                              46.557 16.546 9.308 1.00 16.05
                                                           PROT
                                                           PROT
    ATOM 1852 CA PHE 459
                              47.840 17.174 9.586 1.00 20.28
                                                           PROT
                              48.862 16.072 9.846 1.00 20.26
    ATOM 1853 CB PHE 459
                              48.389 15.055 10.833 1.00 27.22
                                                           PROT
    ATOM 1854 CG PHE 459
    ATOM 1855 CD1 PHE 459
                               47.917 13.822 10.408 1.00 28.01
                                                           PROT
45
                               48.390 15.339 12.204 1.00 40.66
                                                           PROT
    ATOM 1856 CD2 PHE 459
                               47.447 12.876 11.334 1.00 21.78
                                                           PROT
    ATOM 1857 CE1 PHE 459
    ATOM 1858 CE2 PHE 459
                             47.922 14.402 13.140 1.00 25.98
                                                           PROT
    ATOM 1859 CZ PHE 459 47.450 13.172 12.702 1.00 17.63
                                                           PROT
                             48.381 18.152 8.540 1.00 23.03
                                                          PROT
    ATOM 1860 C PHE 459
50
```

```
PROT
                               49.601 18.311 8.416 1.00 27.34
    ATOM 1861 O PHE 459
                               47.480 18.816 7.815 1.00 33.88
                                                              PROT
    ATOM 1862 N GLU 460
                                47.846 19.774 6.767 1.00 36.60
                                                              PROT
    ATOM 1863 CA GLU 460
                                48.930 20.732 7.257 1.00 46.04
                                                              PROT
    ATOM 1864 CB GLU 460
                                                              PROT
                                48.406 21.899 8.054 1.00 67.27
    ATOM 1865 CG GLU 460
                                47.298 22.636 7.339 1.00 71.34
                                                              PROT
    ATOM 1866 CD GLU 460
                                                               PROT
    ATOM 1867 OE1 GLU 460
                                47.448 23.859 7.121 1.00 71.99
    ATOM 1868 OE2 GLU 460
                                46.280 21.993 6.998 1.00 72.73
                                                               PROT
                               48.353 19.037 5.535 1.00 46.31
                                                              PROT
    ATOM 1869 C GLU 460
                               48.642 17.829 5.655 1.00 51.79
    ATOM 1870 O GLU 460
                                                              PROT
10
                                48.461 19.669 4.462 1.00 60.92
                                                              PROT
    ATOM 1871 OT GLU 460
                              47.011 4.539 15.912 1.00 29.38
                                                             LIGA
    ATOM 1872 C1 GC1
                          1
                              51.292 6.537 13.571 1.00 17.11
                                                             LIGA
    ATOM 1873 C2 GC1
                           1
                                                             LIGA
    ATOM 1874 C3 GC1
                              47.393 4.205 14.573 1.00 33.72
                              52.119 6.409 12.400 1.00 19.76
                                                             LIGA
    ATOM 1875 C4 GC1
                          1
15
                                                             LIGA
    ATOM 1876 C5 GC1
                              48,689 4,481 14,089 1,00 25.02
                           1
                              52.344 7.525 11.539 1.00 17.51
                                                             LIGA
    ATOM 1877 C6 GC1
                              49.684 5.122 14.949 1.00 23.99
                                                             LIGA
     ATOM 1878 C7 GC1
                              51.722 8.778 11.873 1.00 20.21
                                                             LIGA
     ATOM 1879 C8 GC1
                              49.283 5.452 16.318 1.00 18.19
                                                             LIGA
     ATOM 1880 C9 GC1
20
                               50.906 8.928 13.018 1.00 15.43
                                                             LIGA
     ATOM 1881 C10 GC1
                           1
                                                             LIGA
                               47.973 5.163 16.779 1.00 30.64
     ATOM 1882 C11 GC1
                           1
                               50.696 7.827 13.850 1.00 25.06
                                                             LIGA
     ATOM 1883 C12 GC1
                           1
                               45.700 4.254 16.325 1.00 28.60
                                                             LIGA
     ATOM 1884 O5 GC1
                           1
                                                             LIGA
                               53.198 7.459 10.291 1.00 20.30
25
     ATOM 1885 C14 GC1
                           1
                                                             LIGA
    ATOM 1886 C15 GC1
                           1
                               45.305 3.866 17.666 1.00 18.51
                               52.423 6.824 9.131 1.00 17.21
                                                             LIGA
     ATOM 1887 C16 GC1
                           1
                                                             LIGA
                               43.816 4.078 17.872 1.00 21.43
     ATOM 1888 C17 GC1
                           1
                                                             LIGA
                               54.514 6.689 10.543 1.00 24.97
     ATOM 1889 C18 GC1
                           1
                               48.994 4.093 12.664 1.00 33.46
                                                             LIGA
     ATOM 1890 C19 GC1
30
                               50.243 6.110 17.278 1.00 27.69
                                                             LIGA
     ATOM 1891 C20 GC1
                           1
                               51.902 9.861 11.086 1.00 23.34
                                                             LIGA
     ATOM 1892 O1 GC1
                           1
     ATOM 1893 C21 GC1
                               51.026 5.430 14.458 1.00 22.49
                                                             LIGA
                           1
                                                             LIGA
                               43.147 3.117 18.247 1.00 18.06
     ATOM 1894 O3 GC1
                           1
                               43.331 5.204 17.665 1.00 28.27
                                                             LIGA
     ATOM 1895 O4 GC1
35
                           1
     END
```

## APPENDIX 8

## TRBGC1.PDB

REMARK TR-beta GC-2 Full length numbering

REMARK refinement resolution: 100.00 - 2.40 A starting r= 0.2602 free\_r= 0.2960

5 REMARK

final r = 0.2532 free\_r = 0.2894

REMARK sg= P3(1)21 a= 68.9 b= 68.9 c= 131.5 alpha= 90 beta= 90 gamma= 120

REMARK theoretical total number of refl. in resol. range: 14710 (100.0%)

REMARK number of unobserved reflections (no entry or |F|=0): 336 ( 2.3 %)

REMARK number of reflections rejected:

0(0.0%)

10 REMARK total number of reflections used:

14374 ( 97.7 % )

REMARK number of reflections in working set:

13656 ( 92.8 % )

REMARK number of reflections in test set:

718 ( 4.9 %)

REMARK

REMARK ALA 199 to ALA 201 from His-tag

15 REMARK

REMARK Four cacodylate-modified cysteines (CYA)

REMARK Cys294, Cys298, Cys388, Cys434

REMARK cacodylate modeled as single arsenic atom

**REMARK** 

20 REMARK side chain of certain residues modeled as ALA due to poor density;

REMARK however, residue name reflects true residue for clarity

**REMARK** 

REMARK amino acid sequence confirmed,

REMARK differing from that reported by Weinberger et. al.

25 REMARK in the following codons:

REMARK 243 Pro - Arg

REMARK 337 lle - Thr

REMARK 451 Leu - Phe

REMARK as reported by Sakurai et. al.

30 REMARK note also correction of initiation codon,

REMARK yielding a polypeptide of 461 amino acids

JRNL AUTH A.SAKURAI, A.NAKAI, L.J. DEGROOT

JRNL TITL STRUCTURAL ANALYSIS OF HUMAN THYROID HORMONE RECEPTOR

35 JRNL TITL2 BETA GENE

JRNL REF MOL.CELL.ENDO. V.71 1990

JRNL AUTH

C.WEINBERGER,

C.C.THOMPSON,R.LEBO,D.J.GRUOL,R.M.EVANS

JRNL TITL THE C-ERB-A GENE ENCODES A THYROID HORMONE

40 RECEPTOR

JRNL REF NATURE

V.324 6098 1986

ATOM 1 CB ALA 199 36.564 26.104 43.169 1.00 73.87 ATOM 2 C ALA 199 34.723 26.996 44.613 1.00 78.22

ATOM 3 O ALA 199 34.741 28.230 44.568 1.00 81.84

45 ATOM 4 N ALA 199 34.389 26.744 42.166 1.00 77.76

ATOM 5 CA ALA 199 35.048 26.165 43.375 1.00 77.98

ATOM 6 N ALA 200 34.428 26.309 45.713 1.00 77.78

```
34.098 26.961 46.984 1.00 77.03
             7 CA ALA 200
     ATOM
                               32.761 27.693 46.865 1.00 79.04
             8 CB ALA 200
     ATOM
             9 C ALA 200
                              34.028 25.897 48.084 1.00 75.79
     ATOM
                              34.877 25.857 48.978 1.00 71.58
     ATOM
             10 O ALA 200
             11 N ALA 201
                              33.005 25.050 48.010 1.00 73.70
5
     ATOM
                               32.838 23.968 48.972 1.00 70.15
             12 CA ALA 201
     ATOM
                               31.468 23.328 48.809 1.00 71.16
             13 CB ALA 201
     ATOM
                               33.934 22.963 48.642 1.00 67.54
             14 C ALA 201
     ATOM
             15 O ALA 201
                               34.218 22.044 49.413 1.00 67.14
     ATOM
                               34.540 23.164 47.476 1.00 62.05
             16 N GLU 202
     ATOM
10
                               35.624 22.325 46.975 1.00 59.45
             17 CA GLU 202
     ATOM
                               35.835 22.621 45.482 1.00 55.12
             18 CB GLU 202
     ATOM
                                36.820 21.716 44.749 1.00 56.25
             19 CG GLU 202
     ATOM
                                36.382 20.260 44.723 1.00 54.99
             20 CD GLU 202
     ATOM
                                35.216 19.990 44.361 1.00 53.83
             21 OE1 GLU 202
     ATOM
15
                                37.210 19.385 45.050 1.00 59.90
             22 OE2 GLU 202
     ATOM
                               36.885 22.674 47.770 1.00 55.96
             23 C GLU 202
     ATOM
                               37.472 21.823 48.435 1.00 52.90
     ATOM
             24 O GLU 202
                               37.282 23.943 47.698 1.00 54.95
             25 N GLU 203
     ATOM
                                38.464 24.434 48.390 1.00 55.59
             26 CA GLU 203
20
     ATOM
             27 CB GLU 203
                                38.632 25.924 48.126 1.00 53.21
     ATOM
                               38.415 24.171 49.894 1.00 56.30
             28 C GLU 203
     ATOM
                               39.445 23.948 50.526 1.00 58.70
             29 O GLU 203
     ATOM
                               37.213 24.193 50.462 1.00 57.14
             30 N LEU 204
     ATOM
             31 CA LEU 204
                               37.038 23.966 51.893 1.00 56.93
25
     ATOM
                               35.658 24.465 52.338 1.00 58.31
             32 CB LEU 204
     ATOM
                                35.348 24.508 53.839 1.00 51.69
     ATOM
             33 CG LEU 204
                                36.314 25.446 54.549 1.00 44.38
     ATOM
             34 CD1 LEU 204
                                33.920 24.986 54.039 1.00 52.44
             35 CD2 LEU 204
     ATOM
                               37.198 22.489 52.246 1.00 58.20
             36 C LEU 204
30
     ATOM
                               37.831 22.155 53.252 1.00 58.99
             37 O LEU 204
     ATOM
                               36.620 21.607 51.431 1.00 58.26
             38 N GLN 205
     ATOM
                                36.736 20.167 51.657 1.00 55.38
             39 CA GLN 205
     ATOM
                                35.993 19.377 50.584 1.00 54.52
             40 CB GLN 205
     ATOM
                                34.498 19.324 50.741 1.00 53.33
             41 CG GLN 205
     ATOM
35
                                33.854 18.520 49.629 1.00 53.40
             42 CD GLN 205
     ATOM
                                33.850 18.939 48.473 1.00 51.68
     ATOM
             43 OE1 GLN 205
                                33.325 17.352 49.968 1.00 51.34
     ATOM
             44 NE2 GLN 205
                               38.200 19.775 51.608 1.00 55.05
             45 C GLN 205
     ATOM
                               38.665 18.964 52.407 1.00 53.63
40
     ATOM
             46 O GLN 205
                               38.918 20.348 50.648 1.00 53.55
     ATOM
             47 N LYS 206
             48 CA LYS 206
                                40.337 20.078 50.493 1.00 57.40
     ATOM
                                40.896 20.814 49.269 1.00 58.94
             49 CB LYS 206
     ATOM
                                40.300 20.375 47.941 1.00 67.73
     ATOM
             50 CG LYS 206
              51 CD LYS 206
                                40.921 21.141 46.781 1.00 72.50
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     ATOM
                               40.346 20.695 45.445 1.00 75.60
              52 CE LYS 206
     ATOM
                               40.945 21.445 44.304 1.00 77.08
     ATOM
              53 NZ LYS 206
              54 C LYS 206
                               41.053 20.559 51.747 1.00 53.98
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                               41.905 19.866 52.300 1.00 53.49
              55 O LYS 206
     ATOM
                               40.680 21.757 52.184 1.00 53.61
     ATOM
              56 N SER 207
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41.254 22.386 53.364 1.00 51.49
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    ATOM
                               40.546 23.715 53.619 1.00 51.01
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             58 CB SER 207
                               41.108 24.383 54.731 1.00 63.00
             59 OG SER 207
    ATOM
                              41.178 21.502 54.616 1.00 49.49
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    ATOM
                               42.073 21.538 55.465 1.00 47.44
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             61 O SER 207
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                              40.117 20.707 54.725 1.00 44.39
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             62 N ILE 208
                               39.938 19.829 55.874 1.00 45.99
             63 CA ILE 208
    ATOM
                               38.421 19.627 56.174 1.00 44.50
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    ATOM
                               38.226 18.801 57.445 1.00 49.37
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             65 CG2 ILE 208
             66 CG1 ILE 208
                               37.766 20.993 56.385 1.00 42.73
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    ATOM
                               36.266 20.941 56.567 1.00 44.13
             67 CD1 ILE 208
    ATOM
             68 C ILE 208
                              40.614 18.477 55.643 1.00 47.80
    ATOM
                              40.735 17.666 56.562 1.00 49.81
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             69 O ILE 208
             70 N GLY 209
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             71 CA GLY 209
                                41.728 16.983 54.107 1.00 46.85
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             72 C GLY 209
                               40.813 15.896 53.573 1.00 48.31
     ATOM
             73 O GLY 209
                               41.203 14.730 53.485 1.00 47.75
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             74 N HIS 210
                              39.582 16.274 53.237 1.00 46.79
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     ATOM
             75 CA HIS 210
                               38.622 15.326 52.686 1.00 47.34
                               37.200 15.739 53.068 1.00 49.39
             76 CB HIS 210
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     ATOM
                              38.796 15.350 51.162 1.00 45.47
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             77 C HIS 210
             78 O HIS 210
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                               38.829 14.176 50.545 1.00 45.76
             79 N LYS 211
     ATOM
                                38.991 14.095 49.090 1.00 43.42
             80 CA LYS 211
     ATOM
             81 CB LYS 211
                               39.892 12.910 48.715 1.00 46.72
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     ATOM
     ATOM
             82 CG LYS 211
                               41.210 12.815 49.497 1.00 56.48
                                42.068 14.089 49.486 1.00 60.93
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                               42.562 14.496 48.103 1.00 61.95
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             84 CE LYS 211
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             85 NZ LYS 211
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                               37.019 12.847 48.557 1.00 33.58
             87 O LYS 211
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                               37.077 14.972 47.828 1.00 35.64
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             88 N PRO 212
                                37.654 16.304 47.584 1.00 38.60
     ATOM
             89 CD PRO 212
                                35.748 14.896 47.211 1.00 38.35
             90 CA PRO 212
     ATOM
                                35.537 16.318 46.682 1.00 38.95
             91 CB PRO 212
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     ATOM
             92 CG PRO 212
                                36.409 17.156 47.604 1.00 42.00
     ATOM
             93 C PRO 212
                               35.635 13.865 46.096 1.00 38.78
     ATOM
             94 O PRO 212
                               36.546 13.714 45.280 1.00 34.64
     ATOM
     ATOM
             95 N GLU 213
                               34.517 13.153 46.077 1.00 40.31
                                34.256 12.160 45.049 1.00 43.87
             96 CA GLU 213
     ATOM
40
                                33.722 10.873 45.684 1.00 45.16
     ATOM
             97 CB GLU 213
     ATOM
             98 CG GLU 213
                                34.616 10.344 46.800 1.00 47.60
             99 CD GLU 213
                                34.404 8.870 47.088 1.00 50.68
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                                 33.240 8.416 47.072 1.00 59.18
             100 OE1 GLU 213
     ATOM
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     ATOM
             101 OE2 GLU 213
                                 35.402 8.167 47.353 1.00 49.06
                                33.234 12.796 44.083 1.00 45.96
             102 C GLU 213
     ATOM
                                32.703 13.876 44.368 1.00 43.13
     ATOM
             103 O GLU 213
     ATOM
             104 N PRO 214
                                32.953 12.154 42.933 1.00 46.52
                                33.459 10.884 42.391 1.00 46.44
             105 CD PRO 214
     ATOM
                                31.995 12.737 41.982 1.00 47.52
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             106 CA PRO 214
     ATOM
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32.040 11.750 40.813 1.00 45.40
            107 CB PRO 214
    ATOM
                               33.445 11.181 40.913 1.00 49.89
            108 CG PRO 214
    ATOM
    ATOM 109 C PRO 214
                              30.564 12.969 42.465 1.00 45.70
                              29.972 12.112 43.121 1.00 44.49
    ATOM 110 O PRO 214
                              30.013 14.136 42.129 1.00 45.24
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                               28.629 14.447 42.483 1.00 49.36
    ATOM 112 CA THR 215
    ATOM 113 CB THR 215
                               28.312 15.949 42.330 1.00 44.86
                                28.253 16.285 40.942 1.00 52.26
    ATOM 114 OG1 THR 215
                                29.387 16.793 42.992 1.00 39.43
    ATOM 115 CG2 THR 215
                              27.791 13.673 41.464 1.00 52.51
    ATOM 116 C THR 215
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                              28.326 13.192 40.465 1.00 53.48
    ATOM 117 O THR 215
                              26.491 13.543 41.712 1.00 58.81
    ATOM 118 N ASP 216
                               25.603 12.810 40.805 1.00 61.51
    ATOM 119 CA ASP 216
            120 CB ASP 216
                               24.150 12.941 41.270 1.00 70.57
    ATOM
                               23.902 12.257 42.595 1.00 78.07
            121 CG ASP 216
15
    ATOM
    ATOM 122 OD1 ASP 216
                               24.042 11.018 42.660 1.00 82.31
                                23.572 12.962 43.571 1.00 86.55
    ATOM 123 OD2 ASP 216
    ATOM 124 C ASP 216
                              25.706 13.277 39.356 1.00 58.42
                              25.695 12.464 38.429 1.00 56.85
    ATOM 125 O ASP 216
                               25.798 14.587 39.167 1.00 54.92
    ATOM 126 N GLU 217
20
                               25.905 15.156 37.833 1.00 53.37
    ATOM
            127 CA GLU 217
    ATOM 128 CB GLU 217
                               25.861 16.682 37.906 1.00 51.02
                               27.211 14.692 37.195 1.00 53.55
    ATOM 129 C GLU 217
                               27.239 14.301 36.027 1.00 54.33
            130 O GLU 217
    ATOM
     ATOM 131 N GLU 218
                               28.290 14.726 37.975 1.00 49.20
25
                               29.593 14.310 37.486 1.00 45.94
    ATOM
            132 CA GLU 218
            133 CB GLU 218
                               30.674 14.601 38.530 1.00 43.43
     ATOM
     ATOM 134 CG GLU 218
                               30.787 16.069 38.878 1.00 40.86
                                31.930 16.347 39.826 1.00 39.88
            135 CD GLU 218
     ATOM
            136 OE1 GLU 218
                                32.000 15.667 40.875 1.00 37.61
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     ATOM
                                32.748 17.250 39.529 1.00 34.01
            137 OE2 GLU 218
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                               29.624 12.838 37.101 1.00 44.71
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     ATOM
                               30.275 12.471 36.130 1.00 45.31
     ATOM
            139 O GLU 218
                              28.935 11.991 37.863 1.00 44.02
            140 N TRP 219
     ATOM
                               28.892 10.572 37.539 1.00 46.97
            141 CA TRP 219
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     ATOM
            142 CB TRP 219
                               28.183 9.762 38.630 1.00 48.42
     ATOM
            143 CG TRP 219
                               29.034 9.473 39.823 1.00 54.61
     ATOM
                                30.167 8.572 39.879 1.00 55.24
            144 CD2 TRP 219
     ATOM
                               30.659 8.610 41.201 1.00 53.67
     ATOM
            145 CE2 TRP 219
            146 CE3 TRP 219
                                30.795 7.745 38.938 1.00 54.55
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     ATOM
                                28.902 10.000 41.074 1.00 55.75
     ATOM
            147 CD1 TRP 219
                                29.868 9.491 41.912 1.00 54.43
     ATOM
            148 NE1 TRP 219
                                31.771 7.846 41.622 1.00 52.54
            149 CZ2 TRP 219
     ATOM
                                31.912 6.975 39.353 1.00 55.17
            150 CZ3 TRP 219
     ATOM
45
     ATOM
            151 CH2 TRP 219
                                32.380 7.038 40.690 1.00 55.59
                              28.167 10.356 36.216 1.00 47.32
            152 C TRP 219
     ATOM
            153 O TRP 219
                              28.433 9.384 35.503 1.00 43.56
     ATOM
     ATOM
            154 N GLU 220
                               27.247 11.259 35.898 1.00 49.91
            155 CA GLU 220
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     ATOM
                               25.274 12.075 34.694 1.00 58.18
            156 CB GLU 220
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24.323 11.876 33.526 1.00 73.13
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                                23.082 12.742 33.630 1.00 80.06
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            158 CD GLU 220
                                22.348 12.619 34.636 1.00 82.12
            159 OE1 GLU 220
    ATOM
            160 OE2 GLU 220
                                22.839 13.545 32.701 1.00 82.78
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                               27.399 10.899 32.443 1.00 49.94
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                               28.232 12.567 33.711 1.00 43.71
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            164 CA LEU 221
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            165 CB LEU 221
     ATOM
            166 CG LEU 221
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     ATOM
                                30.339 15.351 30.922 1.00 36.93
            167 CD1 LEU 221
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                                31.535 16.164 32.949 1.00 24.18
            168 CD2 LEU 221
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                               30.234 11.928 32.505 1.00 43.46
            169 C LEU 221
     ATOM
                               30.618 11.621 31.375 1.00 45.25
            170 O LEU 221
     ATOM
                              30.683 11.342 33.614 1.00 39.09
            171 N ILE 222
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     ATOM
                               31.677 10.273 33.586 1.00 35.47
            172 CA ILE 222
     ATOM
            173 CB ILE 222
                               32.031 9.811 35.037 1.00 33.74
     ATOM
            174 CG2 ILE 222
                               32.822 8.505 35.018 1.00 28.86
     ATOM
                               32.813 10.918 35.745 1.00 33.33
     ATOM
            175 CG1 ILE 222
            176 CD1 ILE 222
                               33.111 10.646 37.199 1.00 34.85
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     ATOM
                              31.139 9.098 32.781 1.00 34.26
            177 C ILE 222
     ATOM
            178 O ILE 222
                              31.877 8.427 32.070 1.00 31.90
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            179 N LYS 223
                               29.840 8.860 32.908 1.00 39.49
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                                29.168 7.775 32.210 1.00 44.43
            180 CA LYS 223
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                               27.696 7.733 32.635 1.00 50.81
            181 CB LYS 223
25
     ATOM
                                26.845 6.693 31.929 1.00 62.51
     ATOM
            182 CG LYS 223
            183 CD LYS 223
                               25.379 6.856 32.313 1.00 72.22
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            184 CE LYS 223
                               24.487 5.855 31.591 1.00 74.55
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                               23.045 6.057 31.925 1.00 75.78
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            186 C LYS 223
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                               29.640 7.078 29.946 1.00 40.36
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                               28.924 9.194 30.257 1.00 39.89
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            189 CA THR 224
                                28.948 9.566 28.850 1.00 39.93
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            190 CB THR 224
                                28.466 11.021 28.680 1.00 40.57
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                                 27.135 11.134 29.197 1.00 39.27
            191 OG1 THR 224
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     ATOM
                                28.480 11.437 27.214 1.00 38.11
            192 CG2 THR 224
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                               30.333 9.433 28.234 1.00 39.96
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            193 C THR 224
                               30.515 8.714 27.248 1.00 36.67
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                               31.303 10.123 28.833 1.00 38.02
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            195 N VAL 225
            196 CA VAL 225
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                                33.565 11.014 29.243 1.00 38.19
            197 CB VAL 225
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                                 34.960 11.162 28.632 1.00 36.77
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            198 CG1 VAL 225
            199 CG2 VAL 225
                                 32.910 12.361 29.406 1.00 41.76
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            200 C VAL 225
                               33.291 8.724 28.302 1.00 37.52
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            201 O VAL 225
                               34.022 8.395 27.364 1.00 36.77
            202 N THR 226
                               33.002 7.904 29.310 1.00 34.02
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                                33.542 6.552 29.350 1.00 34.67
            203 CA THR 226
     ATOM
                                33.237 5.857 30.707 1.00 30.56
            204 CB THR 226
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             205 OG1 THR 226
                                 33.858 6.598 31.768 1.00 32.20
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                                33.775 4.437 30.722 1.00 20.99
            206 CG2 THR 226
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     ATOM
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32.960 5.722 28.211 1.00 36.41
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    ATOM
            208 O THR 226
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                              31.636 5.758 28.073 1.00 39.20
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            210 CA GLU 227
                               30.935 5.020 27.027 1.00 36.93
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                               29.434 5.296 27.111 1.00 38.06
            211 CB GLU 227
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                              31.466 5.409 25.651 1.00 37.69
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           213 O GLU 227
                              31.713 4.544 24.805 1.00 40.94
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                              31.641 6.709 25.439 1.00 32.86
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            214 N ALA 228
                               32.156 7.236 24.177 1.00 32.48
            215 CA ALA 228
    ATOM
           216 CB ALA 228
                               32.285 8.746 24.256 1.00 28.25
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            217 C ALA 228
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                              33.736 6.135 22.747 1.00 37.86
            218 O ALA 228
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           219 N HIS 229
                             34.404 6.611 24.843 1.00 33.58
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            220 CA HIS 229
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                              36.579 6.263 25.921 1.00 33.69
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            222 CG HIS 229
                              37.857 5.489 25.934 1.00 28.39
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            223 CD2 HIS 229
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                               38.804 5.593 24.937 1.00 30.47
           224 ND1 HIS 229
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           225 CE1 HIS 229
            226 NE2 HIS 229
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           227 C HIS 229
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                             36.227 4.071 23.383 1.00 41.49
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                              34.951 3.786 25.216 1.00 38.55
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                               34.823 2.339 25.049 1.00 40.40
    ATOM 230 CA VAL 230
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           231 CB VAL 230
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            232 CG1 VAL 230
                               33.865 0.208 26.041 1.00 39.39
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           233 CG2 VAL 230
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                              34.219 1.934 23.700 1.00 44.28
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                              32.580 2.403 21.961 1.00 47.84
    ATOM 237 CA ALA 231
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    ATOM 240 O ALA 231
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           250 CB ASN 233
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                               39.909 1.765 23.223 1.00 68.35
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            252 OD1 ASN 233
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                              38.934 0.577 19.645 1.00 68.80
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            265 CD GLN 235
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            274 N SER 237
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            280 CA HIS 238
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            281 CB HIS 238
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            293 CZ2 TRP 239
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            294 CZ3 TRP 239
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            297 O TRP 239
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            298 N LYS 240
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            384 CG1 ILE 250
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            452 CG LEU 266
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            486 C SER 270
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            487 O SER 270
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            503 CD2 PHE 272
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     ATOM 513 CG2 THR 273
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     ATOM 518 CB LYS 274
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     ATOM 520 O LYS 274
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            526 CD1 ILE 275
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            560 CG1 ILE 280
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            567 OG1 THR 281
            568 CG2 THR 281
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                               37.435 7.926 13.968 1.00 29.94
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            579 NH2 ARG 282
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            581 O ARG 282
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                                41.448 9.577 17.487 1.00 28.28
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            586 CG2 VAL 283
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            601 OD2 ASP 285
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                              34.679 9.624 18.916 1.00 35.96
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            609 CD2 PHE 286
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     ATOM 611 CE2 PHE 286
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            903 CB GLU 324
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            925 CG2 THR 327
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            927 O THR 327
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     ATOM
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            931 CG LEU 328
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             935 O LEU 328
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     ATOM
             947 CD1 LEU 330
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             948 CD2 LEU 330
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     ATOM
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     ATOM
             955 OD1 ASN 331
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             958 O ASN 331
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            984 O ALA 335
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            986 CA VAL 336
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           988 CG1 VAL 336
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           989 CG2 VAL 336
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                               55.650 -2.309 19.019 1.00 47.42
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     ATOM 993 CA THR 337
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                               59.608 -3.259 18.296 1.00 41.35
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           995 OG1 THR 337
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     ATOM 1003 CD ARG 338
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     ATOM 1004 NE ARG 338
     ATOM 1005 CZ ARG 338
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     ATOM 1006 NH1 ARG 338
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     ATOM 1011 CA GLY 339
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     ATOM 1017 CG GLN 340
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     ATOM 1026 CG LEU 341
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     ATOM 1028 CD2 LEU 341
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     ATOM 1046 C ASN 343
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                               58.085 7.912 12.520 1.00 39.52
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     ATOM 1057 CA LEU 346
                               57.904 8.761 13.692 1.00 36.05
                                57.039 8.048 14.738 1.00 35.72
     ATOM 1058 CB LEU 346
                                55.561 7.864 14.371 1.00 34.89
     ATOM 1059 CG LEU 346
                                54.850 7.132 15.494 1.00 44.09
     ATOM 1060 CD1 LEU 346
     ATOM 1061 CD2 LEU 346
                                54.903 9.213 14.146 1.00 34.84
30
                               59.189 9.264 14.339 1.00 33.52
     ATOM 1062 C LEU 346
                               59.171 10.257 15.066 1.00 35.58
     ATOM 1063 O LEU 346
                               60.299 8.595 14.067 1.00 30.47
     ATOM 1064 N GLY 347
                                61.559 9.017 14.661 1.00 33.01
     ATOM 1065 CA GLY 347
                               61.504 9.069 16.182 1.00 30.72
     ATOM 1066 C GLY 347
35
                               60.967 8.160 16.812 1.00 30.89
     ATOM 1067 O GLY 347
     ATOM 1068 N VAL 348
                               62.051 10.132 16.765 1.00 31.30
     ATOM 1069 CA VAL 348
                                62.084 10.291 18.221 1.00 31.27
     ATOM 1070 CB VAL 348
                                62.843 11.612 18.620 1.00 31.66
     ATOM 1071 CG1 VAL 348
                                62.071 12.841 18.146 1.00 20.19
40
     ATOM 1072 CG2 VAL 348
                                 63.080 11.651 20.118 1.00 24.77
                               60.683 10.273 18.855 1.00 33.84
     ATOM 1073 C VAL 348
                               60.546 10.034 20.050 1.00 29.99
     ATOM 1074 O VAL 348
     ATOM 1075 N VAL 349
                               59.649 10.518 18.049 1.00 33.31
                                58.270 10.495 18.538 1.00 32.23
     ATOM 1076 CA VAL 349
45
                                57.279 10.911 17.415 1.00 32.59
     ATOM 1077 CB VAL 349
     ATOM 1078 CG1 VAL 349
                                 55.837 10.678 17.838 1.00 33.68
                                57.474 12.378 17.103 1.00 32.30
     ATOM 1079 CG2 VAL 349
                               57.931 9.094 19.050 1.00 34.91
     ATOM 1080 C VAL 349
     ATOM 1081 O VAL 349
                               57.133 8.932 19.980 1.00 33.73
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58.551 8.081 18.444 1.00 32.81
    ATOM 1082 N SER 350
                              58.335 6.704 18.853 1.00 30.10
    ATOM 1083 CA SER 350
                              59.041 5.746 17.904 1.00 24.95
    ATOM 1084 CB SER 350
                              58.943 4.417 18.387 1.00 23.16
    ATOM 1085 OG SER 350
    ATOM 1086 C SER 350
                              58.863 6.486 20.266 1.00 31.59
5
                              58.207 5.845 21.086 1.00 37.62
    ATOM 1087 O SER 350
                              60.055 7.007 20.546 1.00 28.60
    ATOM 1088 N ASP 351
    ATOM 1089 CA ASP 351 60.652 6.863 21.867 1.00 29.82
                               62.048 7.491 21.919 1.00 27.49
    ATOM 1090 CB ASP 351
    ATOM 1091 CG ASP 351
                               63.030 6.806 21.000 1.00 30.22
10
    ATOM 1092 OD1 ASP 351
                                63.411 7.412 19.974 1.00 32.61
                                63.422 5.661 21.301 1.00 30.02
    ATOM 1093 OD2 ASP 351
                              59.785 7.548 22.913 1.00 30.63
    ATOM 1094 C ASP 351
                              59.632 7.055 24.027 1.00 29.54
    ATOM 1095 O ASP 351
                               59.222 8.692 22.537 1.00 25.33
    ATOM 1096 N ALA 352
15
                               58.390 9.464 23.432 1.00 28.59
    ATOM 1097 CA ALA 352
                               58.011 10.798 22.788 1.00 20.95
    ATOM 1098 CB ALA 352
    ATOM 1099 C ALA 352
                               57.136 8.695 23.831 1.00 29.69
    ATOM 1100 O ALA 352
                               56.711 8.753 24.982 1.00 30.36
    ATOM 1101 N ILE 353
                              56.557 7.979 22.876 1.00 27.63
20
                               55.345 7.227 23.129 1.00 27.55
    ATOM 1102 CA ILE 353
                               54.611 6.925 21.805 1.00 28.04
    ATOM 1103 CB ILE 353
                              53.329 6.111 22.065 1.00 23.68
    ATOM 1104 CG2 ILE 353
    ATOM 1105 CG1 ILE 353
                               54.269 8.251 21.119 1.00 27.33
    ATOM 1106 CD1 ILE 353
                               53.637 8.105 19.734 1.00 26.23
25
                              55.631 5.943 23.901 1.00 30.88
    ATOM 1107 C ILE 353
                              54.880 5.597 24.814 1.00 31.22
    ATOM 1108 O ILE 353
                               56.710 5.240 23.549 1.00 29.86
    ATOM 1109 N PHE 354
                              57.056 4.022 24.275 1.00 31.08
    ATOM 1110 CA PHE 354
                               58.227 3.274 23.619 1.00 28.80
    ATOM 1111 CB PHE 354
30
                               57.799 2.322 22.523 1.00 28.80
    ATOM 1112 CG PHE 354
    ATOM 1113 CD1 PHE 354
                              57.330 2.804 21.292 1.00 30.96
                                57.811 0.939 22.749 1.00 29.45
    ATOM 1114 CD2 PHE 354
                                56.864 1.909 20.281 1.00 27.12
    ATOM 1115 CE1 PHE 354
                                57.354 0.026 21.761 1.00 25.19
    ATOM 1116 CE2 PHE 354
35
    ATOM 1117 CZ PHE 354
                               56.879 0.518 20.521 1.00 28.09
                               57.398 4.349 25.721 1.00 29.17
    ATOM 1118 C PHE 354
                               57.001 3.625 26.631 1.00 32.62
    ATOM 1119 O PHE 354
                               58.133 5.438 25.925 1.00 23.86
    ATOM 1120 N ASP 355
                               58.508 5.873 27.262 1.00 25.34
    ATOM 1121 CA ASP 355
40
    ATOM 1122 CB ASP 355
                               59.434 7.083 27.180 1.00 21.41
                               60.846 6.708 26.769 1.00 32.08
     ATOM 1123 CG ASP 355
                               61.051 5.595 26.226 1.00 33.58
     ATOM 1124 OD1 ASP 355
                                61.756 7.534 26.970 1.00 33.20
     ATOM 1125 OD2 ASP 355
                              57.254 6.211 28.062 1.00 27.86
    ATOM 1126 C ASP 355
45
                               57.167 5.916 29.252 1.00 32.42
     ATOM 1127 O ASP 355
                               56.276 6.821 27.401 1.00 26.84
     ATOM 1128 N LEU 356
                              55.031 7.164 28.066 1.00 28.66
     ATOM 1129 CA LEU 356
     ATOM 1130 CB LEU 356 54.112 7.953 27.131 1.00 25.37
    ATOM 1131 CG LEU 356
                                52.787 8.427 27.742 1.00 27.61
50
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53.056 9.452 28.842 1.00 25.43
    ATOM 1132 CD1 LEU 356
                                51.924 9.057 26.667 1.00 27.49
    ATOM 1133 CD2 LEU 356
    ATOM 1134 C LEU 356
                               54.334 5.875 28.473 1.00 30.44
                               53.873 5.743 29.601 1.00 31.55
    ATOM 1135 O LEU 356
    ATOM 1136 N GLY 357
                               54.266 4.928 27.536 1.00 32.69
                               53.621 3.652 27.787 1.00 29.87
    ATOM 1137 CA GLY 357
    ATOM 1138 C GLY 357
                               54.239 2.884 28.939 1.00 33.12
    ATOM 1139 O GLY 357
                               53.524 2.268 29.732 1.00 29.41
                               55.570 2.911 29.026 1.00 33.31
    ATOM 1140 N MET 358
    ATOM 1141 CA MET 358
                                56.277 2.217 30.100 1.00 35.87
10
    ATOM 1142 CB MET 358
                                57.794 2.265 29.871 1.00 34.56
    ATOM 1143 CG MET 358
                                58.265 1.608 28.576 1.00 46.43
                               60.073 1.600 28.351 1.00 42.13
    ATOM 1144 SD MET 358
    ATOM 1145 CE MET 358
                               60.429 3.306 28.411 1.00 44.29
    ATOM 1146 C MET 358
                               55.948 2.884 31.434 1.00 33.26
15
                               55.802 2.222 32.453 1.00 36.39
    ATOM 1147 O MET 358
                              55.825 4.202 31.398 1.00 33.31
    ATOM 1148 N SER 359
                               55.533 4.998 32.580 1.00 34.39
    ATOM 1149 CA SER 359
                               55.859 6.463 32.303 1.00 30.84
    ATOM 1150 CB SER 359
    ATOM 1151 OG SER 359
                               55,487 7.265 33,404 1.00 47.14
20
    ATOM 1152 C SER 359
                              54.094 4.897 33.072 1.00 36.43
                              53.833 5.073 34.260 1.00 35.46
    ATOM 1153 O SER 359
                               53.165 4.617 32.156 1.00 36.74
    ATOM 1154 N LEU 360
                               51.750 4.519 32.493 1.00 35.44
    ATOM 1155 CA LEU 360
                               50.889 4.817 31.263 1.00 34.16
25
    ATOM 1156 CB LEU 360
    ATOM 1157 CG LEU 360
                               50.896 6.263 30.751 1.00 34.59
                                50.031 6.353 29.513 1.00 33.53
    ATOM 1158 CD1 LEU 360
    ATOM 1159 CD2 LEU 360
                                50.376 7.211 31.836 1.00 31.69
                              51.324 3.192 33.088 1.00 38.72
    ATOM 1160 C LEU 360
    ATOM 1161 O LEU 360
                               50.185 3.058 33.546 1.00 38.29
30
                              52.227 2.214 33.080 1.00 40.96
    ATOM 1162 N SER 361
    ATOM 1163 CA SER 361
                             51.938 0.897 33.636 1.00 45.67
    ATOM 1164 CB SER 361
                               53.131 -0.044 33.436 1.00 46.45
    ATOM 1165 OG SER 361
                              53.362 -0.296 32.061 1.00 51.81
                              51.628 1.004 35.124 1.00 44.49
    ATOM 1166 C SER 361
35
    ATOM 1167 O SER 361
                              50.724 0.337 35.630 1.00 46.67
                              52.385 1.858 35.809 1.00 41.44
    ATOM 1168 N SER 362
    ATOM 1169 CA SER 362
                              52.231 2.081 37.245 1.00 42.13
                               53.431 2.876 37.779 1.00 42.61
    ATOM 1170 CB SER 362
    ATOM 1171 OG SER 362
                               54.647 2.215 37.492 1.00 51.87
40
                              50.951 2.832 37.610 1.00 38.41
    ATOM 1172 C SER 362
    ATOM 1173 O SER 362
                              50.444 2.700 38.722 1.00 38.01
    ATOM 1174 N PHE 363
                              50.443 3.631 36.672 1.00 34.55
    ATOM 1175 CA PHE 363
                               49.232 4.404 36.906 1.00 32.96
    ATOM 1176 CB PHE 363
                               49.109 5.518 35.859 1.00 31.99
45
                               50.093 6.659 36.058 1.00 29.97
    ATOM 1177 CG PHE 363
    ATOM 1178 CD1 PHE 363
                               49.667 7.872 36.594 1.00 30.61
                              51.445 6.501 35.731 1.00 32.02
    ATOM 1179 CD2 PHE 363
    ATOM 1180 CE1 PHE 363
                               50.579 8.940 36.803 1.00 33.67
                               52.376 7.552 35.934 1.00 30.91
50
    ATOM 1181 CE2 PHE 363
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ATOM 1182 CZ PHE 363
                               51.938 8.777 36.473 1.00 29.33
                              47.973 3.554 36.916 1.00 30.52
    ATOM 1183 C PHE 363
                               46.971 3.947 37.491 1.00 32.19
    ATOM 1184 O PHE 363
                               48.036 2.384 36.283 1.00 33.51
    ATOM 1185 N ASN 364
    ATOM 1186 CA ASN 364
                               46.894 1.471 36.216 1.00 38.03
    ATOM 1187 CB ASN 364
                               46.754 0.711 37.539 1.00 42.32
                               47.824 -0.361 37.713 1.00 53.11
    ATOM 1188 CG ASN 364
    ATOM 1189 OD1 ASN 364
                                47.815 -1.370 37.012 1.00 59.51
    ATOM 1190 ND2 ASN 364
                                48.751 -0.138 38.639 1.00 55.95
                               45.574 2.161 35.871 1.00 31.89
    ATOM 1191 C ASN 364
10
                               44.587 2.027 36.588 1.00 30.28
    ATOM 1192 O ASN 364
                               45.561 2.883 34.751 1.00 27.62
    ATOM 1193 N LEU 365
                               44.365 3.606 34.317 1.00 29.36
    ATOM 1194 CA LEU 365
                               44.738 4.627 33.240 1.00 27.54
    ATOM 1195 CB LEU 365
    ATOM 1196 CG LEU 365
                               45.826 5.659 33.576 1.00 38.91
15
    ATOM 1197 CD1 LEU 365
                                46.115 6.499 32.338 1.00 34.47
                                45.394 6.546 34.743 1.00 34.24
    ATOM 1198 CD2 LEU 365
                               43.264 2.691 33.774 1.00 26.23
    ATOM 1199 C LEU 365
                               43.546 1.648 33.197 1.00 27.06
    ATOM 1200 O LEU 365
    ATOM 1201 N ASP 366
                               42.011 3.074 33.991 1.00 25.23
20
                               40.892 2.307 33.462 1.00 26.07
    ATOM 1202 CA ASP 366
                               39.832 2.008 34.538 1.00 29.68
    ATOM 1203 CB ASP 366
    ATOM 1204 CG ASP 366
                               39.337 3.253 35.261 1.00 35.74
                                39.438 4.371 34.717 1.00 36.78
    ATOM 1205 OD1 ASP 366
                                38.803 3.100 36.378 1.00 41.23
    ATOM 1206 OD2 ASP 366
25
                              40.274 3.100 32.305 1.00 27.70
    ATOM 1207 C ASP 366
    ATOM 1208 O ASP 366
                              40.748 4.191 31.975 1.00 31.94
    ATOM 1209 N ASP 367
                              39.223 2.564 31.693 1.00 29.18
    ATOM 1210 CA ASP 367
                               38.594 3.233 30.560 1.00 32.72
                               37.428 2.395 30.018 1.00 38.04
30
    ATOM 1211 CB ASP 367
    ATOM 1212 CG ASP 367
                               37.855 0.995 29.606 1.00 42.43
                                38.913 0.852 28.956 1.00 35.95
    ATOM 1213 OD1 ASP 367
                                37.115 0.034 29.917 1.00 51.42
     ATOM 1214 OD2 ASP 367
                              38.093 4.631 30.881 1.00 33.71
    ATOM 1215 C ASP 367
                               38.059 5.506 30.013 1.00 38.30
35
    ATOM 1216 O ASP 367
                               37.705 4.852 32.132 1.00 31.06
    ATOM 1217 N THR 368
                              37.199 6.155 32.543 1.00 26.28
    ATOM 1218 CA THR 368
     ATOM 1219 CB THR 368
                                36.537 6.066 33.922 1.00 27.30
     ATOM 1220 OG1 THR 368
                                35.461 5.127 33.861 1.00 33.42
                                36.003 7.423 34.355 1.00 25.16
    ATOM 1221 CG2 THR 368
40
                               38.303 7.194 32.593 1.00 21.13
     ATOM 1222 C THR 368
     ATOM 1223 O THR 368
                               38.133 8.314 32.104 1.00 23.17
     ATOM 1224 N GLU 369
                               39.431 6.816 33.179 1.00 21.32
                                40.565 7.720 33.317 1.00 28.00
     ATOM 1225 CA GLU 369
                                41.582 7.107 34.277 1.00 32.79
    ATOM 1226 CB GLU 369
45
                                40.944 6.804 35.619 1.00 36.29
     ATOM 1227 CG GLU 369
    ATOM 1228 CD GLU 369
                                41.834 6.026 36.546 1.00 41.03
                                42.361 4.967 36.123 1.00 42.05
     ATOM 1229 OE1 GLU 369
     ATOM 1230 OE2 GLU 369
                                41.986 6.458 37.705 1.00 42.03
                               41.201 8.047 31.970 1.00 25.57
    ATOM 1231 C GLU 369
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ATOM 1232 O GLU 369
                               41.626 9.175 31.741 1.00 20.56
                               41.249 7.055 31.080 1.00 25.39
    ATOM 1233 N VAL 370
                                41.794 7.278 29.745 1.00 25.99
    ATOM 1234 CA VAL 370
                               42.005 5.936 28.977 1.00 26.15
    ATOM 1235 CB VAL 370
                                42.450 6.216 27.539 1.00 27.65
    ATOM 1236 CG1 VAL 370
                                43.056 5.086 29.685 1.00 17.70
    ATOM 1237 CG2 VAL 370
    ATOM 1238 C VAL 370
                               40.814 8.164 28.966 1.00 26.49
    ATOM 1239 O VAL 370
                               41.226 9.038 28.202 1.00 28.16
                               39.514 7.950 29.184 1.00 21.01
    ATOM 1240 N ALA 371
                                38.486 8.730 28.510 1.00 19.57
    ATOM 1241 CA ALA 371
10
    ATOM 1242 CB ALA 371
                                37.116 8.136 28.783 1.00 18.62
                               38.512 10.191 28.947 1.00 23.48
    ATOM 1243 C ALA 371
                               38.500 11.103 28.111 1.00 32.67
    ATOM 1244 O ALA 371
                               38.540 10.414 30.256 1.00 22.89
    ATOM 1245 N LEU 372
                                38.560 11.772 30.806 1.00 23.28
    ATOM 1246 CA LEU 372
15
                                38.517 11.709 32.343 1.00 27.76
    ATOM 1247 CB LEU 372
                                37.155 11.306 32.924 1.00 21.18
    ATOM 1248 CG LEU 372
                                37.289 10.891 34.381 1.00 27.64
    ATOM 1249 CD1 LEU 372
                                36.197 12.480 32.763 1.00 20.90
    ATOM 1250 CD2 LEU 372
                               39.804 12.505 30.357 1.00 21.34
    ATOM 1251 C LEU 372
20
                               39.779 13.708 30.086 1.00 23.16
    ATOM 1252 O LEU 372
                               40.896 11.761 30.276 1.00 24.42
     ATOM 1253 N LEU 373
                                42.177 12.302 29.855 1.00 23.78
     ATOM 1254 CA LEU 373
     ATOM 1255 CB LEU 373
                                43.222 11.205 30.007 1.00 22.18
                                44.724 11.456 30.036 1.00 31.52
     ATOM 1256 CG LEU 373
25
                                45.099 12.565 31.001 1.00 31.93
     ATOM 1257 CD1 LEU 373
     ATOM 1258 CD2 LEU 373
                                45.382 10.152 30.460 1.00 30.24
                               42.025 12.757 28.399 1.00 25.69
     ATOM 1259 C LEU 373
                               42.469 13.842 28.025 1.00 30.13
     ATOM 1260 O LEU 373
                               41.370 11.934 27.587 1.00 26.24
     ATOM 1261 N GLN 374
30
     ATOM 1262 CA GLN 374
                                41.151 12.269 26.184 1.00 21.60
                                40.501 11.091 25.444 1.00 24.57
     ATOM 1263 CB GLN 374
     ATOM 1264 CG GLN 374
                                41.428 9.900 25.234 1.00 21.02
                                40.762 8.744 24.501 1.00 22.86
     ATOM 1265 CD GLN 374
                                41.407 7.754 24.174 1.00 24.07
35
     ATOM 1266 OE1 GLN 374
                                39.466 8.865 24.249 1.00 25.59
     ATOM 1267 NE2 GLN 374
                               40.267 13.498 26.070 1.00 20.66
     ATOM 1268 C GLN 374
                               40.518 14.366 25.242 1.00 24.47
     ATOM 1269 O GLN 374
                               39.237 13.579 26.902 1.00 16.26
     ATOM 1270 N ALA 375
                                38.337 14.727 26.870 1.00 17.16
40
     ATOM 1271 CA ALA 375
                                37.156 14.491 27.803 1.00 19.53
     ATOM 1272 CB ALA 375
                               39.056 16.024 27.252 1.00 25.13
     ATOM 1273 C ALA 375
                               38.722 17.100 26.750 1.00 23.81
     ATOM 1274 O ALA 375
                               40.036 15.926 28.156 1.00 24.57
     ATOM 1275 N VAL 376
                                40.796 17.101 28.568 1.00 25.80
     ATOM 1276 CA VAL 376
45
                                41.711 16.792 29.814 1.00 26.48
     ATOM 1277 CB VAL 376
                                42.625 17.971 30.102 1.00 23.20
     ATOM 1278 CG1 VAL 376
                                40.845 16.521 31.044 1.00 19.08
     ATOM 1279 CG2 VAL 376
                               41.653 17.580 27.396 1.00 25.69
     ATOM 1280 C VAL 376
                               41.775 18.780 27.151 1.00 27.87
     ATOM 1281 O VAL 376
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42.249 16.637 26.666 1.00 23.09
     ATOM 1282 N LEU 377
                                43.071 16.982 25.513 1.00 22.86
    ATOM 1283 CA LEU 377
                                43.748 15.730 24.962 1.00 18.50
     ATOM 1284 CB LEU 377
     ATOM 1285 CG LEU 377
                                44.814 15.096 25.867 1.00 22.65
    ATOM 1286 CD1 LEU 377
                                45.144 13.708 25.374 1.00 16.70
 5
                                46.070 15.987 25.901 1.00 19.58
     ATOM 1287 CD2 LEU 377
                               42.197 17.634 24.430 1.00 26.14
     ATOM 1288 C LEU 377
     ATOM 1289 O LEU 377
                               42.579 18.638 23.830 1.00 20.62
                               41.016 17.057 24.208 1.00 28.99
     ATOM 1290 N LEU 378
                                40.076 17.578 23.218 1.00 28.87
     ATOM 1291 CA LEU 378
10
     ATOM 1292 CB LEU 378
                                38.814 16.710 23.182 1.00 26.89
                                37.637 17.167 22.311 1.00 28.83
     ATOM 1293 CG LEU 378
                                38.053 17.273 20.840 1.00 27.97
     ATOM 1294 CD1 LEU 378
     ATOM 1295 CD2 LEU 378
                                 36.496 16.175 22.478 1.00 27.69
                               39.693 19.025 23.504 1.00 31.09
     ATOM 1296 C LEU 378
15
                               39.812 19.883 22.629 1.00 31.77
     ATOM 1297 O LEU 378
                                39.247 19.297 24.729 1.00 31.44
     ATOM 1298 N MET 379
                                38.841 20.649 25.104 1.00 32.62
     ATOM 1299 CA MET 379
     ATOM 1300 CB MET 379
                                37.876 20.603 26.293 1.00 31.45
                                36.586 19.855 26.010 1.00 38.75
20
     ATOM 1301 CG MET 379
     ATOM 1302 SD MET 379
                                35.646 20.541 24.601 1.00 41.27
     ATOM 1303 CE MET 379
                                34.231 19.443 24.609 1.00 35.68
                                39.980 21.613 25.421 1.00 33.72
     ATOM 1304 C MET 379
     ATOM 1305 O MET 379
                                39.940 22.297 26.446 1.00 36.29
                               40.981 21.676 24.543 1.00 34.49
     ATOM 1306 N SER 380
25
                                42.116 22.585 24.721 1.00 33.97
     ATOM 1307 CA SER 380
     ATOM 1308 CB SER 380
                                43.371 22.025 24.061 1.00 31.24
                                43.771 20.814 24.674 1.00 39.42
     ATOM 1309 OG SER 380
                               41.772 23.926 24.088 1.00 39.69
     ATOM 1310 C SER 380
                               41.787 24.069 22.864 1.00 44.64
     ATOM 1311 O SER 380
30
                               41.472 24.907 24.927 1.00 41.04
     ATOM 1312 N SER 381
                                41.090 26.234 24.462 1.00 44.91
     ATOM 1313 CA SER 381
                                40.406 27.004 25.594 1.00 44.50
     ATOM 1314 CB SER 381
                                41.294 27.177 26.678 1.00 45.42
     ATOM 1315 OG SER 381
                               42.231 27.084 23.921 1.00 44.59
35
     ATOM 1316 C SER 381
                               42.012 28.227 23.516 1.00 49.32
     ATOM 1317 O SER 381
     ATOM 1318 N ASP 382
                               43.440 26.541 23.896 1.00 43.75
                                44.571 27.315 23.407 1.00 43.93
     ATOM 1319 CA ASP 382
                                45.817 27.047 24.257 1.00 48.39
     ATOM 1320 CB ASP 382
                                46.319 25.632 24.113 1.00 53.23
     ATOM 1321 CG ASP 382
40
                                 45.590 24.702 24.517 1.00 56.97
     ATOM 1322 OD1 ASP 382
                                 47.440 25.449 23.584 1.00 58.91
     ATOM 1323 OD2 ASP 382
     ATOM 1324 C ASP 382
                               44.900 27.026 21.955 1.00 41.09
                               45.912 27.502 21.446 1.00 40.93
     ATOM 1325 O ASP 382
     ATOM 1326 N ARG 383
                                44.068 26.236 21.287 1.00 42.63
45
     ATOM 1327 CA ARG 383
                                 44.316 25.937 19.876 1.00 43.32
     ATOM 1328 CB ARG 383
                                43.289 24.935 19.331 1.00 42.31
                                43.174 23.619 20.095 1.00 40.83
     ATOM 1329 CG ARG 383
     ATOM 1330 CD ARG 383
                                44.478 22.835 20.139 1.00 38.09
                                 44.271 21.542 20.787 1.00 37.33
50
     ATOM 1331 NE ARG 383
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ATOM 1332 CZ ARG 383
                                45.235 20.690 21.115 1.00 38.35
     ATOM 1333 NH1 ARG 383
                                 46.505 20.972 20.850 1.00 33.70
                                 44.922 19.545 21.704 1.00 35.46
     ATOM 1334 NH2 ARG 383
     ATOM 1335 C ARG 383
                               44.166 27.256 19.127 1.00 44.96
     ATOM 1336 O ARG 383
                               43.214 28.006 19.361 1.00 45.60
     ATOM 1337 N PRO 384
                               45.112 27.574 18.230 1.00 45.33
     ATOM 1338 CD PRO 384
                               46.330 26.852 17.836 1.00 46.85
     ATOM 1339 CA PRO 384
                               45.024 28.830 17.484 1.00 47.37
                               46.323 28.823 16.672 1.00 46.90
     ATOM 1340 CB PRO 384
                               47.257 27.998 17.552 1.00 46.41
     ATOM 1341 CG PRO 384
10
                               43.788 28.910 16.590 1.00 48.29
     ATOM 1342 C PRO 384
     ATOM 1343 O PRO 384
                               43.394 27.927 15.960 1.00 48.34
     ATOM 1344 N GLY 385
                               43.176 30.090 16.552 1.00 49.88
     ATOM 1345 CA GLY 385
                                42.013 30.290 15.712 1.00 50.35
     ATOM 1346 C GLY 385
                               40.669 29.958 16.324 1.00 50.70
15
     ATOM 1347 O GLY 385
                               39.639 30.201 15.697 1.00 53.48
                               40.663 29.404 17.529 1.00 49.04
     ATOM 1348 N LEU 386
                                39.405 29.057 18.182 1.00 50.53
     ATOM 1349 CA LEU 386
                                39.655 28.433 19.558 1.00 45.17
     ATOM 1350 CB LEU 386
     ATOM 1351 CG LEU 386
                                40.245 27.019 19.544 1.00 48.26
20
     ATOM 1352 CD1 LEU 386
                                40.502 26.564 20.970 1.00 41.68
     ATOM 1353 CD2 LEU 386
                                39.285 26.065 18.836 1.00 38.40
                               38.495 30.268 18.319 1.00 52.13
     ATOM 1354 C LEU 386
     ATOM 1355 O LEU 386
                               38.955 31.395 18.476 1.00 53.67
     ATOM 1356 N ALA 387
                               37.193 30.020 18.261 1.00 53.42
25
                                36,225 31.093 18.354 1.00 56.01
    ATOM 1357 CA ALA 387
     ATOM 1358 CB ALA 387
                                35.221 30.976 17.202 1.00 56.47
    ATOM 1359 C ALA 387
                               35.482 31.144 19.681 1.00 55.52
     ATOM 1360 O ALA 387
                               35.491 32.171 20.358 1.00 53.75
     ATOM 1361 N CYS 388
                               34.854 30.038 20.065 1.00 56.03
30
    ATOM 1362 CA CYS 388
                               34.072 30.036 21.312 1.00 59.57
    ATOM 1363 CB CYS 388
                               32.724 29.351 21.089 1.00 59.23
    ATOM 1364 SG CYS 388
                               31.314 30.363 21.641 1.00 58.64
    ATOM 1365 C CYS 388
                               34.846 29.289 22.398 1.00 62.18
    ATOM 1366 O CYS 388
                               34.458 28.190 22.790 1.00 67.88
35
    ATOM 1367 N VAL 389
                               35.955 29.950 22.760 1.00 60.78
    ATOM 1368 CA VAL 389
                                37.005 29.583 23.713 1.00 57.70
    ATOM 1369 CB VAL 389
                                38.202 30.580 23.565 1.00 57.09
    ATOM 1370 CG1 VAL 389
                                39.351 30.194 24.494 1.00 59.03
                                38.671 30.618 22.124 1.00 53.98
40
    ATOM 1371 CG2 VAL 389
    ATOM 1372 C VAL 389
                               36.661 29.515 25.195 1.00 57.77
    ATOM 1373 O VAL 389
                               36.943 28.513 25.851 1.00 60.94
    ATOM 1374 N GLU 390
                               36.102 30.594 25.732 1.00 52.68
    ATOM 1375 CA GLU 390
                                35.738 30.636 27.138 1.00 48.41
    ATOM 1376 CB GLU 390
                                35.001 31.928 27.451 1.00 45.19
45
    ATOM 1377 C GLU 390
                               34.868 29.439 27.459 1.00 47.63
    ATOM 1378 O GLU 390
                               34.986 28.837 28.529 1.00 51.95
    ATOM 1379 N ARG 391
                               34.002 29.082 26.517 1.00 47.11
    ATOM 1380 CA ARG 391 33.099 27.950 26.699 1.00 51.64
                                32.050 27.930 25.588 1.00 54.22
    ATOM 1381 CB ARG 391
50
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30.830 27.094 25.915 1.00 64.20
    ATOM 1382 CG ARG 391
                                29.867 27.074 24.748 1.00 73.80
    ATOM 1383 CD ARG 391
                                28.533 26.622 25.128 1.00 79.76
    ATOM 1384 NE ARG 391
                                27.714 27.298 25.929 1.00 84.27
    ATOM 1385 CZ ARG 391
                                28.090 28.465 26.439 1.00 85.28
    ATOM 1386 NH1 ARG 391
                                26.515 26.809 26.217 1.00 86.84
    ATOM 1387 NH2 ARG 391
    ATOM 1388 C ARG 391
                               33.890 26.644 26.684 1.00 48.18
                               33.504 25.671 27.330 1.00 49.57
    ATOM 1389 O ARG 391
    ATOM 1390 N ILE 392
                              34.987 26.625 25.936 1.00 45.01
    ATOM 1391 CA ILE 392
                               35.835 25.440 25.858 1.00 48.77
10
    ATOM 1392 CB ILE 392
                               36.854 25.565 24.692 1.00 46.45
                               37.798 24.370 24.679 1.00 42.35
    ATOM 1393 CG2 ILE 392
                               36.086 25.664 23.367 1.00 49.69
    ATOM 1394 CG1 ILE 392
    ATOM 1395 CD1 ILE 392
                               36.950 25.897 22.136 1.00 51.09
                              36.570 25.246 27.192 1.00 50.90
    ATOM 1396 C ILE 392
15
    ATOM 1397 O ILE 392
                              36.731 24.118 27.657 1.00 52.21
                               36.999 26.346 27.811 1.00 50.43
    ATOM 1398 N GLU 393
    ATOM 1399 CA GLU 393
                                37.673 26.267 29.101 1.00 50.30
    ATOM 1400 CB GLU 393
                                38.202 27.638 29.531 1.00 53.97
     ATOM 1401 CG GLU 393
                                39.322 28.168 28.658 1.00 62.18
20
                                39.911 29.478 29.168 1.00 67.69
    ATOM 1402 CD GLU 393
    ATOM 1403 OE1 GLU 393
                                40.869 29.977 28.537 1.00 66.42
                                39.423 30.009 30.191 1.00 70.64
    ATOM 1404 OE2 GLU 393
                               36.686 25.765 30.145 1.00 49.31
     ATOM 1405 C GLU 393
                               37.018 24.923 30.980 1.00 49.53
25
     ATOM 1406 O GLU 393
     ATOM 1407 N LYS 394
                               35.468 26.286 30.090 1.00 46.07
                              34.428 25.893 31.022 1.00 45.76
    ATOM 1408 CA LYS 394
                               33.147 26.666 30.727 1.00 43.85
     ATOM 1409 CB LYS 394
     ATOM 1410 C LYS 394
                               34.188 24.391 30.909 1.00 46.69
    ATOM 1411 O LYS 394
                               33.982 23.699 31.911 1.00 49.13
30
                               34.223 23.887 29.679 1.00 46.57
     ATOM 1412 N TYR 395
                                34.014 22.467 29.427 1.00 43.33
     ATOM 1413 CA TYR 395
                                33.818 22.211 27.929 1.00 48.44
     ATOM 1414 CB TYR 395
     ATOM 1415 CG TYR 395
                                32.493 22.710 27.335 1.00 53.83
                                32.302 22.727 25.947 1.00 56.43
     ATOM 1416 CD1 TYR 395
35
                                31.078 23.148 25.374 1.00 59.73
     ATOM 1417 CE1 TYR 395
                                31.434 23.132 28.153 1.00 56.47
     ATOM 1418 CD2 TYR 395
                                30.198 23.559 27.592 1.00 62.60
     ATOM 1419 CE2 TYR 395
                                30.037 23.562 26.200 1.00 63.18
     ATOM 1420 CZ TYR 395
     ATOM 1421 OH TYR 395
                                28.834 23.962 25.635 1.00 64.46
40
                               35.189 21.635 29.938 1.00 37.30
     ATOM 1422 C TYR 395
     ATOM 1423 O TYR 395
                               34.993 20.599 30.564 1.00 34.10
                               36.408 22.091 29.671 1.00 31.92
     ATOM 1424 N GLN 396
                                37.584 21.363 30.120 1.00 34.81
     ATOM 1425 CA GLN 396
                                38.861 21.987 29.560 1.00 32.64
     ATOM 1426 CB GLN 396
45
                                40.114 21.183 29.882 1.00 29.57
     ATOM 1427 CG GLN 396
                                41.370 21.827 29.352 1.00 29.46
     ATOM 1428 CD GLN 396
     ATOM 1429 OE1 GLN 396
                                41.648 22.982 29.649 1.00 34.65
                                42.139 21.088 28.570 1.00 27.21
     ATOM 1430 NE2 GLN 396
                               37.647 21.342 31.647 1.00 37.13
     ATOM 1431 C GLN 396
50
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37.939 20.302 32.236 1.00 37.36
    ATOM 1432 O GLN 396
    ATOM 1433 N ASP 397
                               37.371 22.484 32.284 1.00 38.61
                               37.393 22.555 33.742 1.00 40.37
    ATOM 1434 CA ASP 397
                               37.099 23.973 34.240 1.00 40.51
    ATOM 1435 CB ASP 397
    ATOM 1436 CG ASP 397
                                38.130 24.974 33.772 1.00 43.77
    ATOM 1437 OD1 ASP 397
                                39.330 24.632 33.775 1.00 46.50
                                37.750 26.109 33.422 1.00 51.34
    ATOM 1438 OD2 ASP 397
                               36.352 21.601 34.295 1.00 38.62
    ATOM 1439 C ASP 397
                               36.515 21.034 35.372 1.00 39.20
    ATOM 1440 O ASP 397
                               35.282 21.423 33.540 1.00 37.84
    ATOM 1441 N SER 398
10
                               34.221 20.524 33.942 1.00 37.80
    ATOM 1442 CA SER 398
    ATOM 1443 CB SER 398
                               33.039 20.669 32.984 1.00 34.28
    ATOM 1444 OG SER 398
                                31.981 19.815 33.360 1.00 46.60
                               34.752 19.082 33.939 1.00 38.41
    ATOM 1445 C SER 398
                               34.372 18.274 34.787 1.00 39.98
    ATOM 1446 O SER 398
15
                               35.630 18.772 32.987 1.00 34.82
    ATOM 1447 N PHE 399
    ATOM 1448 CA PHE 399
                                36.213 17.433 32.885 1.00 35.96
    ATOM 1449 CB PHE 399
                                36.809 17.181 31.493 1.00 35.75
                                35.775 16.936 30.419 1.00 39.30
    ATOM 1450 CG PHE 399
                                35.640 17.826 29.344 1.00 39.86
    ATOM 1451 CD1 PHE 399
20
    ATOM 1452 CD2 PHE 399
                                34.936 15.819 30.487 1.00 36.81
                                34.674 17.607 28.330 1.00 41.25
    ATOM 1453 CE1 PHE 399
                                33.962 15.577 29.488 1.00 43.61
    ATOM 1454 CE2 PHE 399
    ATOM 1455 CZ PHE 399
                               33.829 16.480 28.402 1.00 40.34
25
     ATOM 1456 C PHE 399
                               37.306 17.217 33.921 1.00 33.48
                               37.406 16.139 34.512 1.00 26.86
    ATOM 1457 O PHE 399
                               38.132 18.239 34.118 1.00 31.47
    ATOM 1458 N LEU 400
                                39.213 18.162 35.086 1.00 37.41
     ATOM 1459 CA LEU 400
     ATOM 1460 CB LEU 400
                                40.051 19.441 35.038 1.00 34.24
                                40.934 19.574 33.788 1.00 35.10
     ATOM 1461 CG LEU 400
30
                                41,469 20,991 33,651 1.00 26,60
     ATOM 1462 CD1 LEU 400
                                42.077 18.569 33.884 1.00 29.44
     ATOM 1463 CD2 LEU 400
                               38.666 17.931 36.491 1.00 38.84
     ATOM 1464 C LEU 400
                               39.137 17.049 37.205 1.00 40.38
     ATOM 1465 O LEU 400
     ATOM 1466 N LEU 401
                               37.654 18.703 36.870 1.00 42.79
35
                                37.056 18.584 38.197 1.00 43.48
     ATOM 1467 CA LEU 401
     ATOM 1468 CB LEU 401
                                35.997 19.675 38.406 1.00 44.73
                                35.322 19.737 39.779 1.00 51.39
     ATOM 1469 CG LEU 401
                                36.359 20.002 40.866 1.00 50.11
     ATOM 1470 CD1 LEU 401
     ATOM 1471 CD2 LEU 401
                                 34.273 20.834 39.778 1.00 49.30
40
                               36.433 17.215 38.409 1.00 41.62
     ATOM 1472 C LEU 401
     ATOM 1473 O LEU 401
                               36.563 16.622 39.482 1.00 45.14
                               35.744 16.712 37.389 1.00 37.92
     ATOM 1474 N ALA 402
                                35.115 15.402 37.484 1.00 29.90
     ATOM 1475 CA ALA 402
     ATOM 1476 CB ALA 402
                                34.196 15.187 36.297 1.00 30.70
45
                               36.203 14.336 37.508 1.00 28.88
     ATOM 1477 C ALA 402
     ATOM 1478 O ALA 402
                               36.083 13.322 38.188 1.00 32.14
     ATOM 1479 N PHE 403
                               37.274 14.588 36.764 1.00 31.07
                              38.402 13.656 36.661 1.00 29.90
     ATOM 1480 CA PHE 403
                                39.396 14.178 35.605 1.00 27.03
50
     ATOM 1481 CB PHE 403
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ATOM 1482 CG PHE 403
                                40.434 13.146 35.140 1.00 26.97
                                41.362 13.509 34.149 1.00 25.55
     ATOM 1483 CD1 PHE 403
     ATOM 1484 CD2 PHE 403
                                40.475 11.841 35.664 1.00 19.75
                                42.331 12.588 33.679 1.00 27.90
     ATOM 1485 CE1 PHE 403
                                41.441 10.899 35.206 1.00 22.56
     ATOM 1486 CE2 PHE 403
 5
     ATOM 1487 CZ PHE 403
                                42.371 11.273 34.210 1.00 22.24
                               39.081 13.523 38.023 1.00 28.82
     ATOM 1488 C PHE 403
     ATOM 1489 O PHE 403
                               39.313 12.413 38.495 1.00 26.00
     ATOM 1490 N GLU 404
                               39.405 14.652 38.652 1.00 30.25
     ATOM 1491 CA GLU 404
                                40.039 14.627 39.966 1.00 34.03
10
     ATOM 1492 CB GLU 404
                                40.264 16.046 40.497 1.00 39.45
                                40.987 16.076 41.839 1.00 47.68
     ATOM 1493 CG GLU 404
                                41.062 17.465 42.446 1.00 54.02
     ATOM 1494 CD GLU 404
     ATOM 1495 OE1 GLU 404
                                41.607 18.380 41.796 1.00 57.27
     ATOM 1496 OE2 GLU 404
                                 40.573 17.638 43.585 1.00 63.85
15
     ATOM 1497 C GLU 404
                               39.164 13.860 40.960 1.00 36.01
                               39.661 12.997 41.701 1.00 38.64
     ATOM 1498 O GLU 404
     ATOM 1499 N HIS 405
                              37.870 14.168 40.975 1.00 29.56
     ATOM 1500 CA HIS 405
                               36.949 13.508 41.892 1.00 31.69
                               35.534 14.077 41.757 1.00 33.75
20
     ATOM 1501 CB HIS 405
     ATOM 1502 CG HIS 405
                               35.401 15.498 42.213 1.00 34.75
                                36.308 16.361 42.730 1.00 34.58
     ATOM 1503 CD2 HIS 405
                                34.207 16.187 42.146 1.00 32.43
     ATOM 1504 ND1 HIS 405
                                34.385 17.414 42.598 1.00 36.15
     ATOM 1505 CE1 HIS 405
                                35.650 17.549 42.960 1.00 39.84
25
     ATOM 1506 NE2 HIS 405
     ATOM 1507 C HIS 405
                              36.904 12.013 41.673 1.00 34.21
                              36.700 11.247 42.624 1.00 37.06
     ATOM 1508 O HIS 405
     ATOM 1509 N TYR 406
                               37.081 11.594 40.419 1.00 30.83
     ATOM 1510 CA TYR 406
                                37.059 10.173 40.093 1.00 28.85
                                37.018 9.959 38.575 1.00 31.48
     ATOM 1511 CB TYR 406
30
     ATOM 1512 CG TYR 406
                                36.879 8.490 38.181 1.00 23.49
     ATOM 1513 CD1 TYR 406
                                 35.683 7.798 38.397 1.00 19.42
     ATOM 1514 CE1 TYR 406
                                35.556 6.427 38.059 1.00 23.80
     ATOM 1515 CD2 TYR 406
                                 37.950 7.794 37.624 1.00 21.81
                                37.838 6.421 37.278 1.00 24.64
35
    ATOM 1516 CE2 TYR 406
                                36.639 5.753 37.503 1.00 21.56
     ATOM 1517 CZ TYR 406
                                36.537 4.404 37.186 1.00 24.96
     ATOM 1518 OH TYR 406
     ATOM 1519 C TYR 406
                               38.318 9.526 40.638 1.00 24.24
     ATOM 1520 O TYR 406
                               38,308 8,375 41,050 1,00 27,08
                              39.407 10.278 40.617 1.00 25.76
     ATOM 1521 N ILE 407
40
     ATOM 1522 CA ILE 407
                               40.688 9.799 41.105 1.00 33.75
                               41.815 10.822 40.796 1.00 34.23
     ATOM 1523 CB ILE 407
     ATOM 1524 CG2 ILE 407
                               43.121 10.400 41.435 1.00 32.46
     ATOM 1525 CG1 ILE 407
                               41.959 10.972 39.275 1.00 43.30
45
     ATOM 1526 CD1 ILE 407
                                42.267 9.677 38.523 1.00 40.40
                              40.620 9.556 42.613 1.00 39.03
     ATOM 1527 C ILE 407
     ATOM 1528 O ILE 407
                              41.192 8.583 43.107 1.00 35.18
     ATOM 1529 N ASN 408
                               39.916 10.440 43.335 1.00 37.25
                              39.778 10.292 44.777 1.00 37.01
     ATOM 1530 CA ASN 408
50
    ATOM 1531 CB ASN 408
                                39.099 11.514 45.400 1.00 32.27
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39.887 12.790 45.187 1.00 33.56
     ATOM 1532 CG ASN 408
                                41.118 12.785 45.225 1.00 31.99
    ATOM 1533 OD1 ASN 408
    ATOM 1534 ND2 ASN 408
                                39.182 13.903 44.996 1.00 31.23
                               38.961 9.046 45.055 1.00 38.14
    ATOM 1535 C ASN 408
                               39.303 8.243 45.920 1.00 42.16
    ATOM 1536 O ASN 408
    ATOM 1537 N TYR 409
                               37.874 8.894 44.303 1.00 35.62
                               37.002 7.733 44.412 1.00 35.91
    ATOM 1538 CA TYR 409
    ATOM 1539 CB TYR 409
                               35.929 7.804 43.323 1.00 34.41
                               35.196 6.495 43.066 1.00 38.73
    ATOM 1540 CG TYR 409
    ATOM 1541 CD1 TYR 409
                                34.266 5.982 43.980 1.00 41.34
10
    ATOM 1542 CE1 TYR 409
                                33.600 4.745 43.741 1.00 47.16
                                35.461 5.752 41.907 1.00 46.20
    ATOM 1543 CD2 TYR 409
    ATOM 1544 CE2 TYR 409
                                34.814 4.518 41.651 1.00 50.74
    ATOM 1545 CZ TYR 409
                               33.891 4.023 42.573 1.00 50.88
    ATOM 1546 OH TYR 409
                               33.262 2.816 42.302 1.00 53.14
15
    ATOM 1547 C TYR 409
                               37.827 6.459 44.240 1.00 38.16
    ATOM 1548 O TYR 409
                               37.806 5.561 45.082 1.00 41.83
                               38.551 6.399 43.125 1.00 42.25
    ATOM 1549 N ARG 410
    ATOM 1550 CA ARG 410
                               39.410 5.272 42.765 1.00 42.83
                               40.029 5.540 41.392 1.00 36.83
20
    ATOM 1551 CB ARG 410
                               39.055 5.397 40.249 1.00 34.32
    ATOM 1552 CG ARG 410
                               39.134 3.996 39.681 1.00 36.62
    ATOM 1553 CD ARG 410
                               40.420 3.787 39.013 1.00 38.64
    ATOM 1554 NE ARG 410
                               40.832 2.625 38.517 1.00 35.73
    ATOM 1555 CZ ARG 410
                               40.068 1.548 38.617 1.00 33.17
25
    ATOM 1556 NH1 ARG 410
    ATOM 1557 NH2 ARG 410
                                42.006 2.544 37.916 1.00 32.70
                               40.520 5.039 43.780 1.00 46.67
    ATOM 1558 C ARG 410
                               40.900 3.901 44.053 1.00 41.78
    ATOM 1559 O ARG 410
    ATOM 1560 N LYS 411
                              41.026 6.140 44.325 1.00 52.99
    ATOM 1561 CA LYS 411 42.109 6.141 45.298 1.00 58.32
30
    ATOM 1562 CB LYS 411
                               41.565 5.956 46.731 1.00 64.99
    ATOM 1563 CG LYS 411
                               40.660 4.763 46.977 1.00 70.48
    ATOM 1564 CD LYS 411
                               40.034 4.866 48.364 1.00 77.18
    ATOM 1565 CE LYS 411
                               39.053 3.732 48.625 1.00 84.30
                               38.392 3.865 49.958 1.00 86.48
35
    ATOM 1566 NZ LYS 411
                              43.238 5.163 45.000 1.00 56.66
    ATOM 1567 C LYS 411
                              43.329 4.075 45.575 1.00 55.47
    ATOM 1568 O LYS 411
    ATOM 1569 N HIS 412
                              44.091 5.582 44.070 1.00 54.67
    ATOM 1570 CA HIS 412
                             45.266 4.823 43.657 1.00 48.67
                              45.878 5.442 42.393 1.00 43.14
    ATOM 1571 CB HIS 412
40
    ATOM 1572 CG HIS 412
                               45.073 5.218 41.156 1.00 41.36
    ATOM 1573 CD2 HIS 412
                             44.084 5.952 40.584 1.00 35.44
    ATOM 1574 ND1 HIS 412 45.220 4.093 40.364 1.00 38.19
                               44.357 4.150 39.363 1.00 34.75
    ATOM 1575 CE1 HIS 412
    ATOM 1576 NE2 HIS 412
                             43.659 5.263 39.474 1.00 35.52
45
                              46.264 4.932 44.793 1.00 46.35
    ATOM 1577 C HIS 412
                              46.326 5.951 45.479 1.00 42.73
    ATOM 1578 O HIS 412
    ATOM 1579 N HIS 413
                              47.049 3.883 44.993 1.00 48.92
                             48.040 3.903 46.052 1.00 53.15
    ATOM 1580 CA HIS 413
                             48.148 2.515 46.688 1.00 55.27
50
    ATOM 1581 CB HIS 413
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46.843 2.015 47.238 1.00 58.77
     ATOM 1582 CG HIS 413
     ATOM 1583 CD2 HIS 413
                               46.138 0.892 46.977 1.00 61.65
     ATOM 1584 ND1 HIS 413
                               46.108 2.726 48.161 1.00 60.31
                               45.003 2.061 48.445 1.00 63.01
     ATOM 1585 CE1 HIS 413
     ATOM 1586 NE2 HIS 413
                               44.993 0.942 47.743 1.00 62.93
 5
     ATOM 1587 C HIS 413
                              49.359 4.364 45.456 1.00 53.19
                              50.335 3.617 45.390 1.00 54.93
     ATOM 1588 O HIS 413
     ATOM 1589 N VAL 414
                               49.343 5.612 44.999 1.00 53.77
                                50.487 6.282 44.389 1.00 51.06
     ATOM 1590 CA VAL 414
                                50.374 6.305 42.838 1.00 51.49
     ATOM 1591 CB VAL 414
10
                                51.603 6.958 42.231 1.00 45.22
     ATOM 1592 CG1 VAL 414
                               50,210 4.891 42.304 1.00 52.67
     ATOM 1593 CG2 VAL 414
     ATOM 1594 C VAL 414
                               50.444 7.724 44.894 1.00 54.28
     ATOM 1595 O VAL 414
                               49.418 8.401 44.774 1.00 55.49
     ATOM 1596 N THR 415
                               51.547 8.190 45.467 1.00 56.28
15
     ATOM 1597 CA THR 415
                                51.610 9.550 45.986 1.00 57.83
     ATOM 1598 CB THR 415
                                52.874 9.756 46.858 1.00 59.64
                               52.922 11.115 47.311 1.00 66.69
     ATOM 1599 OG1 THR 415
     ATOM 1600 CG2 THR 415
                                54.137 9.436 46.067 1.00 59.42
     ATOM 1601 C THR 415
                               51.599 10.577 44.855 1.00 56.98
20
     ATOM 1602 O THR 415
                               52.176 10.345 43.789 1.00 55.70
     ATOM 1603 N HIS 416
                              50.936 11.707 45.093 1.00 57.44
     ATOM 1604 CA HIS 416
                               50.835 12.786 44.108 1.00 57.34
                               52.207 13.425 43.875 1.00 61.35
     ATOM 1605 CB HIS 416
25
     ATOM 1606 CG HIS 416
                               52.860 13.940 45.123 1.00 69.78
     ATOM 1607 CD2 HIS 416
                                54.049 13.633 45.695 1.00 71.42
                              52,283 14,901 45,922 1,00 72,49
     ATOM 1608 ND1 HIS 416
     ATOM 1609 CE1 HIS 416
                               53.087 15.165 46.938 1.00 75.50
     ATOM 1610 NE2 HIS 416
                               54.165 14.410 46.819 1.00 73.91
                              50.301 12.260 42.773 1.00 53.79
30
     ATOM 1611 C HIS 416
     ATOM 1612 O HIS 416
                              50.769 12.667 41.710 1.00 52.81
     ATOM 1613 N PHE 417
                               49.318 11.366 42.824 1.00 48.05
     ATOM 1614 CA PHE 417
                                48.769 10.784 41.610 1.00 47.99
                               47.652 9.799 41.940 1.00 46.11
     ATOM 1615 CB PHE 417
                                47.314 8.868 40.791 1.00 44.27
35
     ATOM 1616 CG PHE 417
     ATOM 1617 CD1 PHE 417
                                48.155 7.796 40.481 1.00 41.79
     ATOM 1618 CD2 PHE 417
                                46.179 9.091 40.003 1.00 40.23
     ATOM 1619 CE1 PHE 417
                                47.872 6.936 39.386 1.00 44.30
                                45.874 8.248 38.907 1.00 36.80
     ATOM 1620 CE2 PHE 417
                               46.725 7.167 38.595 1.00 40.69
     ATOM 1621 CZ PHE 417
40
                               48.227 11.824 40.625 1.00 46.69
     ATOM 1622 C PHE 417
     ATOM 1623 O PHE 417
                               48.551 11.787 39.436 1.00 43.35
     ATOM 1624 N TRP 418
                               47.410 12.746 41.124 1.00 45.14
     ATOM 1625 CA TRP 418
                               46.821 13.775 40.276 1.00 44.89
     ATOM 1626 CB TRP 418
                               45.808 14.604 41.077 1.00 42.24
45
                                45.096 15.646 40.259 1.00 47.11
     ATOM 1627 CG TRP 418
     ATOM 1628 CD2 TRP 418
                                44.186 15.417 39.159 1.00 46.98
     ATOM 1629 CE2 TRP 418
                                43.786 16.678 38.676 1.00 48.94
                                43.676 14.261 38.548 1.00 45.23
     ATOM 1630 CE3 TRP 418
     ATOM 1631 CD1 TRP 418
                                45.204 17.003 40.387 1.00 46.24
50
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44.425 17.637 39.448 1.00 50.63
    ATOM 1632 NE1 TRP 418
                                42.891 16.839 37.598 1.00 45.46
     ATOM 1633 CZ2 TRP 418
                                42.780 14.411 37.468 1.00 44.50
     ATOM 1634 CZ3 TRP 418
    ATOM 1635 CH2 TRP 418
                                42.403 15.696 37.009 1.00 47.55
                               47.862 14.676 39.598 1.00 43.88
 5
    ATOM 1636 C TRP 418
                               47.834 14.842 38.383 1.00 43.17
    ATOM 1637 O TRP 418
    ATOM 1638 N PRO 419
                               48.788 15.281 40.369 1.00 43.55
                                49.006 15.290 41.826 1.00 41.52
    ATOM 1639 CD PRO 419
                               49,787 16.135 39.725 1.00 41.48
    ATOM 1640 CA PRO 419
    ATOM 1641 CB PRO 419
10
                                50.626 16.627 40.912 1.00 39.21
                                49.593 16.667 42.017 1.00 39.25
    ATOM 1642 CG PRO 419
                               50.616 15.363 38.701 1.00 36.28
    ATOM 1643 C PRO 419
                               50.940 15.882 37.638 1.00 37.08
     ATOM 1644 O PRO 419
                               50.959 14.124 39.033 1.00 35.96
    ATOM 1645 N LYS 420
                                51.742 13.281 38.132 1.00 40.82
    ATOM 1646 CA LYS 420
15
                               52.094 11.945 38.792 1.00 40.78
    ATOM 1647 CB LYS 420
     ATOM 1648 CG LYS 420
                                53.086 12.046 39.933 1.00 48.62
                                53.391 10.668 40.497 1.00 55.12
     ATOM 1649 CD LYS 420
                               54.395 10.741 41.635 1.00 53.26
    ATOM 1650 CE LYS 420
    ATOM 1651 NZ LYS 420
                               54.719 9.388 42.152 1.00 52.69
20
                               50.957 13.005 36.860 1.00 40.29
    ATOM 1652 C LYS 420
     ATOM 1653 O LYS 420
                               51.516 12.989 35.764 1.00 39.66
     ATOM 1654 N LEU 421
                               49.658 12.786 37.023 1.00 38.33
                              48.784 12.507 35.903 1.00 37.60
     ATOM 1655 CA LEU 421
                                47.417 12.074 36.428 1.00 43.66
     ATOM 1656 CB LEU 421
25
                                46.386 11.479 35.474 1.00 46.50
     ATOM 1657 CG LEU 421
                                46.946 10.253 34.770 1.00 45.15
    ATOM 1658 CD1 LEU 421
                                45.154 11.107 36.279 1.00 51.31
     ATOM 1659 CD2 LEU 421
                               48.661 13.747 35.014 1.00 39.59
     ATOM 1660 C LEU 421
     ATOM 1661 O LEU 421
                               48.599 13.638 33.791 1.00 40.66
30
                               48.642 14.928 35.623 1.00 39.57
     ATOM 1662 N LEU 422
                                48.545 16.170 34.867 1.00 38.63
     ATOM 1663 CA LEU 422
     ATOM 1664 CB LEU 422
                                48.313 17.357 35.802 1.00 41.79
                                46.996 17.407 36.581 1.00 42.74
     ATOM 1665 CG LEU 422
                                47.010 18.606 37.515 1.00 42.89
     ATOM 1666 CD1 LEU 422
35
                                45.823 17.494 35.628 1.00 39.27
     ATOM 1667 CD2 LEU 422
                               49.808 16.410 34.039 1.00 40.47
     ATOM 1668 C LEU 422
     ATOM 1669 O LEU 422
                               49.747 17.029 32.979 1.00 47.83
     ATOM 1670 N MET 423
                               50.949 15.936 34.519 1.00 34.27
     ATOM 1671 CA MET 423
                                52.187 16.103 33.774 1.00 35.25
40
                                53.403 15.716 34.622 1.00 32.56
     ATOM 1672 CB MET 423
                                53.675 16.654 35.774 1.00 40.70
     ATOM 1673 CG MET 423
     ATOM 1674 SD MET 423
                                55.226 16.278 36.597 1.00 47.65
                                54.920 14.601 37.163 1.00 47.16
     ATOM 1675 CE MET 423
                               52.164 15.254 32.502 1.00 35.13
45
     ATOM 1676 C MET 423
     ATOM 1677 O MET 423
                               52.934 15.499 31.570 1.00 29.85
                               51.285 14.252 32.482 1.00 31.56
     ATOM 1678 N LYS 424
                              51.152 13.384 31.316 1.00 32.29
     ATOM 1679 CA LYS 424
                                50.373 12.115 31.681 1.00 30.56
     ATOM 1680 CB LYS 424
                                51.106 11.178 32.631 1.00 30.07
     ATOM 1681 CG LYS 424
50
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52.248 10.482 31.938 1.00 33.22
    ATOM 1682 CD LYS 424
                               53.059 9.593 32.875 1.00 28.75
    ATOM 1683 CE LYS 424
    ATOM 1684 NZ LYS 424
                               53.868 10.383 33.833 1.00 31.01
                              50.435 14.150 30.197 1.00 29.26
    ATOM 1685 C LYS 424
    ATOM 1686 O LYS 424
                              50.719 13.944 29.030 1.00 30.22
5
                               49.514 15.036 30.573 1.00 23.53
    ATOM 1687 N VAL 425
    ATOM 1688 CA VAL 425
                              48.792 15.849 29.601 1.00 28.91
    ATOM 1689 CB VAL 425
                               47.808 16.829 30.295 1.00 29.44
                               47.148 17.737 29.273 1.00 28.81
    ATOM 1690 CG1 VAL 425
                               46.744 16.049 31.057 1.00 31.22
    ATOM 1691 CG2 VAL 425
10
    ATOM 1692 C VAL 425
                               49.822 16.669 28.831 1.00 32.03
    ATOM 1693 O VAL 425
                               49.771 16.769 27.605 1.00 31.95
    ATOM 1694 N THR 426
                               50.763 17.247 29.570 1.00 33.61
    ATOM 1695 CA THR 426
                              51.821 18.057 28.995 1.00 30.76
    ATOM 1696 CB THR 426
                               52.678 18.695 30.105 1.00 32.34
15
    ATOM 1697 OG1 THR 426
                               51.842 19.535 30.912 1.00 33.07
                               53.812 19.533 29.514 1.00 25.40
    ATOM 1698 CG2 THR 426
                               52.712 17.225 28.086 1.00 32.53
    ATOM 1699 C THR 426
    ATOM 1700 O THR 426
                               53.113 17.686 27.014 1.00 35.19
                              53.022 16.003 28.507 1.00 28.83
20
    ATOM 1701 N ASP 427
    ATOM 1702 CA ASP 427
                               53.858 15.130 27.695 1.00 35.12
                               54.273 13.880 28.476 1.00 39.14
    ATOM 1703 CB ASP 427
    ATOM 1704 CG ASP 427
                               55.122 14.212 29.693 1.00 45.80
    ATOM 1705 OD1 ASP 427
                                56.052 15.034 29.556 1.00 41.97
    ATOM 1706 OD2 ASP 427
                                54.869 13.642 30.775 1.00 50.06
25
                              53.124 14.726 26.422 1.00 33.94
    ATOM 1707 C ASP 427
    ATOM 1708 O ASP 427
                              53.737 14.617 25.362 1.00 38.02
    ATOM 1709 N LEU 428
                               51.818 14.512 26.529 1.00 27.15
                               51.013 14.148 25.373 1.00 29.99
    ATOM 1710 CA LEU 428
                               49.602 13.719 25.802 1.00 22.49
    ATOM 1711 CB LEU 428
30
                               49.541 12.285 26.359 1.00 25.54
    ATOM 1712 CG LEU 428
                                48.210 12.021 27.037 1.00 20.60
    ATOM 1713 CD1 LEU 428
                                49.785 11.303 25.224 1.00 17.24
    ATOM 1714 CD2 LEU 428
                               50.947 15.305 24.381 1.00 28.94
    ATOM 1715 C LEU 428
    ATOM 1716 O LEU 428
                               50.941 15.088 23.174 1.00 31.26
35
    ATOM 1717 N ARG 429
                               50.910 16.531 24.887 1.00 27.64
    ATOM 1718 CA ARG 429
                               50.877 17.694 24.011 1.00 28.13
                                50.584 18.969 24.800 1.00 29.59
    ATOM 1719 CB ARG 429
    ATOM 1720 CG ARG 429
                                49.224 18.980 25.455 1.00 34.85
    ATOM 1721 CD ARG 429
                                48.951 20.314 26.118 1.00 47.18
40
                                47.657 20.358 26.797 1.00 57.93
    ATOM 1722 NE ARG 429
    ATOM 1723 CZ ARG 429
                                46.473 20.193 26.200 1.00 63.62
    ATOM 1724 NH1 ARG 429
                               46.402 19.972 24.889 1.00 60.71
                                45.356 20.257 26.919 1.00 62.38
     ATOM 1725 NH2 ARG 429
                               52.229 17.819 23.304 1.00 29.81
    ATOM 1726 C ARG 429
45
                               52.294 18.209 22.143 1.00 30.81
     ATOM 1727 O ARG 429
     ATOM 1728 N MET 430
                               53.305 17.482 24.008 1.00 29.64
                               54.639 17.545 23.422 1.00 34.72
     ATOM 1729 CA MET 430
                              55.716 17.323 24.485 1.00 34.97
     ATOM 1730 CB MET 430
     ATOM 1731 CG MET 430
                               55.864 18.480 25.451 1.00 45.34
50
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ATOM 1732 SD MET 430
                                56.162 20.050 24.596 1.00 52.55
                                57.598 19.639 23.589 1.00 55.56
     ATOM 1733 CE MET 430
                               54.778 16.500 22.325 1.00 34.01
    ATOM 1734 C MET 430
     ATOM 1735 O MET 430
                               55.440 16.733 21.318 1.00 37.29
                              54.161 15.340 22.533 1.00 29.99
    ATOM 1736 N ILE 431
 5
                               54.197 14.279 21.545 1.00 28.82
     ATOM 1737 CA ILE 431
                               53.523 12.984 22.095 1.00 27.39
    ATOM 1738 CB ILE 431
                               53.260 11.989 20.956 1.00 23.87
    ATOM 1739 CG2 ILE 431
                                54.414 12.386 23.201 1.00 25.56
    ATOM 1740 CG1 ILE 431
                                53.850 11.155 23.896 1.00 17.29
    ATOM 1741 CD1 ILE 431
10
                              53.450 14.785 20.301 1.00 29.49
    ATOM 1742 C ILE 431
                              53.908 14.603 19.174 1.00 24.19
    ATOM 1743 O ILE 431
                               52.311 15.435 20.524 1.00 25.25
    ATOM 1744 N GLY 432
    ATOM 1745 CA GLY 432
                                51.542 15.971 19.419 1.00 30.38
    ATOM 1746 C GLY 432
                               52.334 16.997 18.614 1.00 32.75
15
    ATOM 1747 O GLY 432
                               52.410 16.895 17.387 1.00 36.38
                               52.930 17.974 19.294 1.00 26.77
     ATOM 1748 N ALA 433
     ATOM 1749 CA ALA 433
                                53.711 19.012 18.625 1.00 26.48
                                54.182 20.047 19.631 1.00 19.90
    ATOM 1750 CB ALA 433
    ATOM 1751 C ALA 433
                               54.902 18.407 17.890 1.00 30.73
20
                               55.207 18.787 16.760 1.00 31.60
     ATOM 1752 O ALA 433
                               55.582 17.467 18.537 1.00 33.22
     ATOM 1753 N CYS 434
     ATOM 1754 CA CYS 434
                                56.728 16.801 17.914 1.00 34.34
     ATOM 1755 CB CYS 434
                                57.339 15.808 18.895 1.00 35.20
                                59.191 15.745 18.798 1.00 54.48
    ATOM 1756 SG CYS 434
25
                               56.313 16.052 16.636 1.00 34.09
     ATOM 1757 C CYS 434
                               57.095 15.937 15.679 1.00 34.89
     ATOM 1758 O CYS 434
     ATOM 1759 N HIS 435
                               55.088 15.545 16.642 1.00 34.30
                               54.570 14.818 15.501 1.00 35.44
     ATOM 1760 CA HIS 435
     ATOM 1761 CB HIS 435
                               53.296 14.061 15.886 1.00 31.76
30
                               52.587 13.469 14.715 1.00 32.03
     ATOM 1762 CG HIS 435
                                52.735 12.277 14.092 1.00 28.61
     ATOM 1763 CD2 HIS 435
                                51.665 14.177 13.970 1.00 28.48
     ATOM 1764 ND1 HIS 435
                                51.284 13.453 12.941 1.00 33.27
     ATOM 1765 CE1 HIS 435
                                51.920 12.284 12.985 1.00 31.57
35
     ATOM 1766 NE2 HIS 435
                               54.311 15.750 14.319 1.00 32.74
     ATOM 1767 C HIS 435
                               54.504 15.363 13.175 1.00 32.87
     ATOM 1768 O HIS 435
     ATOM 1769 N ALA 436
                               53.881 16.975 14.608 1.00 31.01
     ATOM 1770 CA ALA 436
                                53.628 17.966 13.571 1.00 29.91
                                53.221 19.290 14.197 1.00 21.23
40
     ATOM 1771 CB ALA 436
                               54.911 18.135 12.769 1.00 33.86
     ATOM 1772 C ALA 436
                               54.892 18.128 11.541 1.00 36.10
     ATOM 1773 O ALA 436
     ATOM 1774 N SER 437
                               56.030 18.266 13.483 1.00 35.19
                                57.344 18.426 12.871 1.00 33.03
     ATOM 1775 CA SER 437
                                58.389 18.720 13.941 1.00 35.31
45
     ATOM 1776 CB SER 437
                                59.681 18.782 13.373 1.00 44.99
     ATOM 1777 OG SER 437
                               57.758 17.178 12.100 1.00 38.39
     ATOM 1778 C SER 437
                               58.374 17.269 11.034 1.00 37.54
     ATOM 1779 O SER 437
     ATOM 1780 N ARG 438
                               57.427 16.012 12.642 1.00 37.32
                                57.762 14.754 11.992 1.00 39.30
     ATOM 1781 CA ARG 438
50
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ATOM 1782 CB ARG 438
                                57.517 13.572 12.941 1.00 42.97
                                58.542 13.436 14.059 1.00 41.72
    ATOM 1783 CG ARG 438
                                59.926 13.212 13.484 1.00 45.23
    ATOM 1784 CD ARG 438
                                59.961 12.050 12.601 1.00 45.66
    ATOM 1785 NE ARG 438
                                60.935 11.804 11.731 1.00 49.71
    ATOM 1786 CZ ARG 438
5
                                61.961 12.641 11.627 1.00 50.91
    ATOM 1787 NH1 ARG 438
                                 60.885 10.727 10.960 1.00 46.86
    ATOM 1788 NH2 ARG 438
                               56.939 14.565 10.725 1.00 42.37
    ATOM 1789 C ARG 438
                               57.311 13.794 9.841 1.00 40.58
    ATOM 1790 O ARG 438
                               55.816 15.269 10.645 1.00 42.25
    ATOM 1791 N PHE 439
10
                                54.957 15.170 9.479 1.00 42.81
    ATOM 1792 CA PHE 439
                                53.593 15.790 9.771 1.00 42.18
    ATOM 1793 CB PHE 439
                                52.594 15.597 8.656 1.00 42.48
    ATOM 1794 CG PHE 439
                                52.173 14.312 8.295 1.00 47.09
    ATOM 1795 CD1 PHE 439
                                52.086 16.696 7.961 1.00 39.76
    ATOM 1796 CD2 PHE 439
15
                                51.256 14.110 7.234 1.00 49.17
    ATOM 1797 CE1 PHE 439
                                51.174 16.524 6.896 1.00 45.10
    ATOM 1798 CE2 PHE 439
                                50.751 15.225 6.532 1.00 46.36
    ATOM 1799 CZ PHE 439
                               55.626 15.905 8.322 1.00 44.79
    ATOM 1800 C PHE 439
    ATOM 1801 O PHE 439
                               55.596 15.444 7.181 1.00 40.26
20
                               56,236 17.049 8.629 1.00 42.77
    ATOM 1802 N LEU 440
                                56.927 17.839 7.621 1.00 42.96
    ATOM 1803 CA LEU 440
                                57.421 19.156 8.216 1.00 37.19
     ATOM 1804 CB LEU 440
     ATOM 1805 CG LEU 440
                                56.348 20.117 8.725 1.00 36.97
     ATOM 1806 CD1 LEU 440
                                57.020 21.338 9.321 1.00 33.65
25
                                55.411 20.519 7.572 1.00 35.42
     ATOM 1807 CD2 LEU 440
                               58.106 17.063 7.053 1.00 45.47
     ATOM 1808 C LEU 440
                               58.421 17.191 5.876 1.00 52.48
     ATOM 1809 O LEU 440
                              58.760 16.266 7.890 1.00 49.15
     ATOM 1810 N HIS 441
                               59.893 15.473 7.435 1.00 54.76
     ATOM 1811 CA HIS 441
30
                               60.723 14.964 8.624 1.00 56.68
     ATOM 1812 CB HIS 441
                               61.515 16.026 9.323 1.00 62.73
     ATOM 1813 CG HIS 441
                                62.851 16.166 9.508 1.00 65.73
     ATOM 1814 CD2 HIS 441
                                60.929 17.098 9.966 1.00 66.01
     ATOM 1815 ND1 HIS 441
                               61.871 17.845 10.518 1.00 65.55
     ATOM 1816 CE1 HIS 441
35
     ATOM 1817 NE2 HIS 441
                                63.044 17.306 10.258 1.00 60.09
                              59.417 14.292 6.589 1.00 55.93
     ATOM 1818 C HIS 441
                              60.084 13.908 5.630 1.00 57.33
     ATOM 1819 O HIS 441
                               58.271 13.716 6.948 1.00 57.81
     ATOM 1820 N MET 442
     ATOM 1821 CA MET 442
                                57.712 12.585 6.203 1.00 59.11
40
                                56.562 11.924 6.978 1.00 55.93
     ATOM 1822 CB MET 442
     ATOM 1823 CG MET 442
                                56.961 11.246 8.276 1.00 58.52
     ATOM 1824 SD MET 442
                                55.564 10.420 9.105 1.00 60.99
     ATOM 1825 CE MET 442
                                54.430 11.779 9.350 1.00 52.61
     ATOM 1826 C MET 442
                                57.178 13.065 4.854 1.00 60.31
45
     ATOM 1827 O MET 442
                                57.279 12.369 3.846 1.00 58.18
     ATOM 1828 N LYS 443
                               56.608 14.266 4.863 1.00 61.45
                                56.038 14.871 3.669 1.00 64.90
     ATOM 1829 CA LYS 443
                                55,434 16,232 4,035 1,00 64,40
     ATOM 1830 CB LYS 443
     ATOM 1831 CG LYS 443
                                54.589 16.872 2.945 1.00 69.12
50
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ATOM 1832 CD LYS 443
                               54.064 18.250 3.363 1.00 71.14
                               53.138 18.183 4.575 1.00 73.43
    ATOM 1833 CE LYS 443
                               52.668 19.534 5.015 1.00 67.97
    ATOM 1834 NZ LYS 443
                              57.112 15.030 2.585 1.00 67.29
    ATOM 1835 C LYS 443
                              56.800 15.218 1.406 1.00 67.90
    ATOM 1836 O LYS 443
5
    ATOM 1837 N VAL 444
                              58.373 14.941 2.996 1.00 66.57
    ATOM 1838 CA VAL 444
                               59.501 15.064 2.078 1.00 64.76
                               60.618 15.940 2.693 1.00 62.76
    ATOM 1839 CB VAL 444
    ATOM 1840 CG1 VAL 444
                               61.767 16.092 1.712 1.00 64.00
                               60.062 17.301 3.072 1.00 59.27
    ATOM 1841 CG2 VAL 444
10
                              60.091 13.693 1.744 1.00 68.61
    ATOM 1842 C VAL 444
                               60.145 13.294 0.577 1.00 70.60
    ATOM 1843 O VAL 444
    ATOM 1844 N GLU 445
                               60.520 12.972 2.775 1.00 70.71
    ATOM 1845 CA GLU 445
                               61.129 11.653 2.609 1.00 71.45
    ATOM 1846 CB GLU 445
                               61.808 11.233 3.916 1.00 72.36
15
                              60.181 10.547 2.148 1.00 71.46
    ATOM 1847 C GLU 445
                              60.588 9.390 2.042 1.00 73.02
    ATOM 1848 O GLU 445
    ATOM 1849 N CYS 446
                              58.925 10.895 1.871 1.00 71.12
    ATOM 1850 CA CYS 446
                               57.945 9.901 1.419 1.00 70.83
                               57.031 9.485 2.581 1.00 71.05
    ATOM 1851 CB CYS 446
20
                               57.845 8.593 3.925 1.00 72.83
    ATOM 1852 SG CYS 446
    ATOM 1853 C CYS 446
                              57.081 10.390 0.261 1.00 71.91
    ATOM 1854 O CYS 446
                              56.776 11.582 0.155 1.00 72.06
    ATOM 1855 N PRO 447
                              56.673 9.470 -0.635 1.00 73.12
                               56.967 8.026 -0.671 1.00 72.88
    ATOM 1856 CD PRO 447
25
                               55.837 9.825 -1.784 1.00 74.22
    ATOM 1857 CA PRO 447
    ATOM 1858 CB PRO 447
                               55.717 8.500 -2.537 1.00 72.98
                               57.015 7.790 -2.161 1.00 74.77
    ATOM 1859 CG PRO 447
    ATOM 1860 C PRO 447
                              54.479 10.343 -1.330 1.00 75.94
    ATOM 1861 O PRO 447
                              53.754 9.652 -0.616 1.00 76.67
30
    ATOM 1862 N THR 448
                              54.145 11.558 -1.755 1.00 76.91
    ATOM 1863 CA THR 448 52.879 12.197 -1.403 1.00 78.24
    ATOM 1864 CB THR 448
                               52.647 13.459 -2.261 1.00 81.33
    ATOM 1865 OG1 THR 448
                              52.552 13.087 -3.643 1.00 84.46
                              53.802 14.444 -2.089 1.00 83.51
    ATOM 1866 CG2 THR 448
35
    ATOM 1867 C THR 448
                              51.676 11.270 -1.580 1.00 77.42
    ATOM 1868 O THR 448
                               50.662 11.413 -0.894 1.00 77.65
    ATOM 1869 N GLU 449
                               51.795 10.319 -2.502 1.00 76.29
     ATOM 1870 CA GLU 449
                              50.720 9.375 -2.783 1.00 75.03
    ATOM 1871 CB GLU 449
                               51.048 8.572 -4.043 1.00 74.62
40
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                               50.445 8.421 -1.622 1.00 73.49
     ATOM 1873 O GLU 449
                               49.310 7.973 -1.442 1.00 70.24
     ATOM 1874 N LEU 450
                              51.477 8.113 -0.840 1.00 70.80
    ATOM 1875 CA LEU 450
                               51.327 7.194 0.285 1.00 68.82
                               52.693 6.644 0.705 1.00 71.91
    ATOM 1876 CB LEU 450
45
     ATOM 1877 CG LEU 450
                               53.428 5.795 -0.336 1.00 76.62
     ATOM 1878 CD1 LEU 450
                               54.799 5.414 0.195 1.00 77.95
     ATOM 1879 CD2 LEU 450
                              52.617 4.546 -0.662 1.00 76.46
                              50.636 7.818 1.492 1.00 66.22
    ATOM 1880 C LEU 450
                               50.501 7.181 2.540 1.00 66.01
    ATOM 1881 O LEU 450
50
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ATOM 1882 N PHE 451
                               50.189 9.060 1.342 1.00 61.96
                               49.513 9.750 2.428 1.00 58.44
     ATOM 1883 CA PHE 451
                               50.006 11.204 2.528 1.00 61.34
     ATOM 1884 CB PHE 451
     ATOM 1885 CG PHE 451
                               51.466 11.343 2.923 1.00 63.02
     ATOM 1886 CD1 PHE 451
                                52.488 10.888 2.077 1.00 62.92
                                51.812 11.932 4.146 1.00 63.07
     ATOM 1887 CD2 PHE 451
                                53.855 11.029 2.437 1.00 65.12
     ATOM 1888 CE1 PHE 451
                                53.167 12.085 4.531 1.00 64.66
     ATOM 1889 CE2 PHE 451
                               54.195 11.628 3.673 1.00 67.12
     ATOM 1890 CZ PHE 451
                               48.005 9.756 2.219 1.00 56.41
     ATOM 1891 C PHE 451
10
                               47.501 10.471 1.350 1.00 56.56
     ATOM 1892 O PHE 451
                               47.260 8.954 3.009 1.00 53.28
     ATOM 1893 N PRO 452
                               47.678 8.027 4.076 1.00 50.46
     ATOM 1894 CD PRO 452
                               45.797 8.910 2.866 1.00 50.26
     ATOM 1895 CA PRO 452
     ATOM 1896 CB PRO 452
                               45.388 7.976 4.000 1.00 49.19
15
                               46.558 7.010 4.039 1.00 45.89
     ATOM 1897 CG PRO 452
                               45.183 10.305 2.974 1.00 49.62
     ATOM 1898 C PRO 452
     ATOM 1899 O PRO 452
                               45.727 11.176 3.644 1.00 52.35
                               44.034 10.530 2.313 1.00 51.50
     ATOM 1900 N PRO 453
                               43.257 9.585 1.494 1.00 49.66
20
     ATOM 1901 CD PRO 453
                               43.354 11.830 2.335 1.00 50.89
     ATOM 1902 CA PRO 453
                               42.101 11.559 1.506 1.00 51.49
     ATOM 1903 CB PRO 453
                               42.600 10.524 0.521 1.00 50.82
     ATOM 1904 CG PRO 453
                               43.030 12.405 3.706 1.00 50.99
     ATOM 1905 C PRO 453
     ATOM 1906 O PRO 453
                               43.264 13.588 3.953 1.00 54.17
25
     ATOM 1907 N LEU 454
                               42.479 11.576 4.592 1.00 51.21
     ATOM 1908 CA LEU 454
                               42.112 12.034 5.936 1.00 47.17
                               41.305 10.951 6.660 1.00 44.44
     ATOM 1909 CB LEU 454
                               40.748 11.283 8.050 1.00 41.33
     ATOM 1910 CG LEU 454
                                39.838 12.504 7.978 1.00 35.93
30
     ATOM 1911 CD1 LEU 454
                                39.986 10.072 8.587 1.00 34.79
     ATOM 1912 CD2 LEU 454
                               43.363 12.380 6.733 1.00 42.25
     ATOM 1913 C LEU 454
                               43.387 13.357 7.475 1.00 40.82
     ATOM 1914 O LEU 454
                               44,399 11.567 6.565 1.00 39.29
     ATOM 1915 N PHE 455
                               45.674 11.774 7.240 1.00 41.81
     ATOM 1916 CA PHE 455
35
                               46.655 10.679 6.802 1.00 47.22
     ATOM 1917 CB PHE 455
                               48.045 10.800 7.407 1.00 56.97
     ATOM 1918 CG PHE 455
     ATOM 1919 CD1 PHE 455
                                48.220 10.990 8.785 1.00 57.23
     ATOM 1920 CD2 PHE 455
                                49.180 10.645 6.597 1.00 59.40
40
     ATOM 1921 CE1 PHE 455
                                49.522 11.030 9.362 1.00 56.58
     ATOM 1922 CE2 PHE 455
                                50.487 10.682 7.149 1.00 61.80
                               50.656 10.870 8.541 1.00 59.94
     ATOM 1923 CZ PHE 455
                               46.203 13.161 6.892 1.00 45.12
     ATOM 1924 C PHE 455
     ATOM 1925 O PHE 455
                               46.558 13.944 7.779 1.00 39.95
                               46.236 13.471 5.592 1.00 43.92
45
     ATOM 1926 N LEU 456
                               46.704 14.767 5.123 1.00 44.08
     ATOM 1927 CA LEU 456
     ATOM 1928 CB LEU 456
                               46.748 14.795 3.593 1.00 50.20
                               47.796 13.921 2.903 1.00 55.79
     ATOM 1929 CG LEU 456
                                47.527 13.869 1.408 1.00 54.70
     ATOM 1930 CD1 LEU 456
50
     ATOM 1931 CD2 LEU 456
                                49.187 14.473 3.193 1.00 53.01
```

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45.782 15.871 5.616 1.00 44.65
    ATOM 1932 C LEU 456
                              46.219 16.987 5.887 1.00 45.93
    ATOM 1933 O LEU 456
                               44.500 15.549 5.726 1.00 44.56
    ATOM 1934 N GLU 457
                               43.498 16.504 6.175 1.00 46.37
    ATOM 1935 CA GLU 457
    ATOM 1936 CB GLU 457
                               42.138 15.854 6.133 1.00 50.16
5
                               43.759 17.039 7.579 1.00 43.60
    ATOM 1937 C GLU 457
                               43.867 18.245 7.795 1.00 42.69
    ATOM 1938 O GLU 457
                               43.847 16.117 8.528 1.00 43.21
    ATOM 1939 N VAL 458
                               44.064 16.446 9.930 1.00 44.98
    ATOM 1940 CA VAL 458
    ATOM 1941 CB VAL 458
                               44.020 15.159 10.802 1.00 44.83
10
                                44.180 15.510 12.277 1.00 49.72
    ATOM 1942 CG1 VAL 458
                                42.708 14.427 10.567 1.00 40.89
    ATOM 1943 CG2 VAL 458
                               45.368 17.178 10.209 1.00 42.72
    ATOM 1944 C VAL 458
                               45.393 18.139 10.974 1.00 42.88
    ATOM 1945 O VAL 458
                               46.451 16.743 9.574 1.00 44.53
    ATOM 1946 N PHE 459
15
                               47.741 17.366 9.823 1.00 48.18
     ATOM 1947 CA PHE 459
                               48.784 16.269 10.064 1.00 43.60
    ATOM 1948 CB PHE 459
                               48.374 15.276 11.133 1.00 40.79
    ATOM 1949 CG PHE 459
                                47.835 14.032 10.783 1.00 41.01
    ATOM 1950 CD1 PHE 459
    ATOM 1951 CD2 PHE 459
                                48.471 15.613 12.492 1.00 39.48
20
                                47.387 13.118 11.776 1.00 40.62
    ATOM 1952 CE1 PHE 459
                                48.032 14.715 13.506 1.00 36.87
    ATOM 1953 CE2 PHE 459
                               47.489 13.463 13.146 1.00 36.39
     ATOM 1954 CZ PHE 459
     ATOM 1955 C PHE 459
                              48.234 18.348 8.763 1.00 52.71
                               49.336 18.878 8.877 1.00 51.34
    ATOM 1956 O PHE 459
25
                               47.397 18.594 7.752 1.00 59.56
     ATOM 1957 N GLU 460
                              47.695 19.509 6.647 1.00 66.14
     ATOM 1958 CA GLU 460
                                47.818 20.944 7.158 1.00 67.76
     ATOM 1959 CB GLU 460
                                46.536 21.511 7.724 1.00 78.99
    ATOM 1960 CG GLU 460
                                46.680 22.965 8.116 1.00 86.08
     ATOM 1961 CD GLU 460
30
                                47.014 23.786 7.237 1.00 87.62
    ATOM 1962 OE1 GLU 460
                                46.460 23.289 9.301 1.00 91.63
     ATOM 1963 OE2 GLU 460
     ATOM 1964 C GLU 460
                               48.940 19.163 5.836 1.00 69.17
                               48.784 18.759 4.660 1.00 69.49
     ATOM 1965 O GLU 460
                                 50.057 19.298 6.379 1.00 76.70
    ATOM 1966 OXT GLU 460
35
                             47.283 4.313 16.972 1.00 44.70
     ATOM 1967 C1 TRI
                        1
                              51.052 6.807 13.814 1.00 34.01
     ATOM 1968 C2 TRI
                         1
                             47.289 4.043 15.500 1.00 37.90
     ATOM 1969 C3 TRI
                         1
                              51.936 6.615 12.728 1.00 33.38
     ATOM 1970 C4 TRI
                          1
                             48.462 4.501 14.746 1.00 46.53
40
     ATOM 1971 C5 TRI
                          1
                              52.294 7.653 11.847 1.00 42.90
     ATOM 1972 C6 TRI
                          1
                              49.577 5.179 15.334 1.00 34.63
     ATOM 1973 C7 TRI
                          1
                              51.717 9.015 12.071 1.00 38.34
     ATOM 1974 C8 TRI
                         1
     ATOM 1975 C9 TRI
                             49.492 5.383 16.723 1.00 43.89
                          1
                              50.779 9.237 13.172 1.00 40.43
     ATOM 1976 C10 TRI
                         1
45
     ATOM 1977 C11 TRI 1
                              48.354 4.960 17.533 1.00 41.82
                              50.449 8.116 14.055 1.00 35.64
     ATOM 1978 C12 TRI
                         1
                            46.287 3.725 17.959 1.00 36.78
     ATOM 1979 C13 TRI 1
     ATOM 1980 C15 TRI 1 44.825 4.150 17.865 1.00 40.69
                             48.684 4.002 12.609 1.00 40.26
50
     ATOM 1981 I1 TRI 1
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53.597 7.174 10.336 1.00 46.70
     ATOM 1982 I2 TRI
                         1
                             51.362 6.218 17.644 1.00 36.54
     ATOM 1983 I3 TRI
                         1
                              44.546 5.255 17.329 1.00 54.78
     ATOM 1984 O3 TRI
                         1
                              50.831 5.617 14.667 1.00 28.44
    ATOM 1985 O2 TRI
                              52.207 10.160 11.342 1.00 43.65
     ATOM 1986 O1 TRI
                          1
     ATOM 1987 O4 TRI
                              44.021 3.333 18.352 1.00 42.95
                          1
                              60.548 16.977 16.916 1.00 65.97
                                                             AS
             1 AS CAC 501
     ATOM
                              27.863 16.627 16.796 1.00 89.34
                                                             AS
     ATOM
             2 AS CAC 502
                              29.889 28.698 21.811 1.00100.00
             3 AS CAC 503
                                                             AS
     ATOM
             4 AS CAC 504
                              33.547 24.203 8.880 1.00100.00
                                                             AS
10
     ATOM
                              42.365 8.872 4.597 1.00 53.88
             5 O HOH 505
                                                           HOH
     ATOM
             6 O HOH 506
                              33.545 30.973 24.585 1.00 40.33
                                                            HOH
     ATOM
             7 O HOH 507
                              37.040 1.824 12.671 1.00 61.87
                                                            HOH
     ATOM
                              44.105 4.635 6.023 1.00 40.68
                                                           HOH
             8 O HOH 508
     ATOM
                              52.686 13.817 -6.263 1.00 54.00
             9 O HOH 509
                                                            HOH
15
     ATOM
                              50.186 12.691 -5.997 1.00 55.36
                                                            HOH
             10 O HOH 510
     ATOM
             11 O HOH 511
                              49.278 18.540 14.006 1.00 34.79
                                                             HOH
     ATOM
                              25.541 28.885 21.206 1.00 55.42
                                                             HOH
     ATOM
             12 O HOH 512
             13 O HOH 513
                              27.346 31.063 27.398 1.00 58.30
                                                             HOH
     ATOM
             14 O HOH 514
                              40.790 19.192 39.234 1.00 50.35
                                                             HOH
20
     ATOM
             15 O HOH 515
                              37.467 0.637 37.293 1.00 37.46
                                                            HOH
     ATOM
                              36.155 3.879 47.189 1.00 61.37
             16 O HOH 516
                                                            HOH
     ATOM
             17 O HOH 517
                              35.410 5.865 50.995 1.00 63.46
                                                            HOH
     ATOM
                              33.622 5.440 47.570 1.00 53.87
                                                            HOH
     ATOM
             18 O HOH 518
25
             19 O HOH 519
                              64.787 6.888 11.882 1.00 51.15
                                                            HOH
     ATOM
             20 O HOH 520
                              61.109 -8.688 27.722 1.00 61.70
                                                             HOH
     ATOM
                              49.869 -5.472 30.343 1.00 40.50
                                                             HOH
     ATOM
             21 O HOH 521
                              43.786 -0.987 26.878 1.00 52.16
                                                             HOH
     ATOM
             22 O HOH 522
             23 O HOH 523
                              41.604 2.361 26.985 1.00 47.90
                                                             HOH
     ATOM
                               54.405 6.361 39.795 1.00 56.56
                                                             HOH
             24 O HOH 524
30
     ATOM
                              46.088 0.770 33.095 1.00 74.24
             25 O HOH 525
                                                             HOH
     ATOM
                              50.481 16.245 15.314 1.00 28.99
             26 O HOH 526
                                                             HOH
     ATOM
                               59.788 14.863 21.416 1.00 50.02
             27 O HOH 527
                                                             HOH
     ATOM
                              49.282 19.490 32.191 1.00 41.61
             28 O HOH 528
                                                             HOH
     ATOM
             29 O HOH 529
                               56.683 10.961 26.733 1.00 34.20
                                                             HOH
35
     ATOM
             30 O HOH 530
                               56.701 9.852 30.561 1.00 51.24
                                                             HOH
     ATOM
                              26.487 13.273 30.591 1.00 43.94
     ATOM
             31 O HOH 531
                                                             HOH
                              27.019 25.052 28.330 1.00 54.97
                                                             HOH
     ATOM
             32 O HOH 532
                               50.689 1.918 29.551 1.00 30.63
                                                             HOH
             33 O HOH 533
     ATOM
                               47.867 0.200 31.330 1.00 43.14
                                                             HOH
40
     ATOM
             34 O HOH 534
                               61.434 -0.721 23.218 1.00 49.83
                                                             HOH
     ATOM
             35 O HOH 535
             36 O HOH 536
                               41.969 20.017 20.894 1.00 27.00
                                                             HOH
     ATOM
                              46.897 16.244 15.992 1.00 31.50
                                                             HOH
             37 O HOH 537
     ATOM
     ATOM
             38 O HOH 538
                               29.796 16.276 27.000 1.00 38.52
                                                             HOH
             39 O HOH 539
                               47.853 23.205 20.217 1.00 44.39
                                                             HOH
45
     ATOM
                              40.956 24.775 31.717 1.00 50.36
                                                             HOH
             40 O HOH 540
     ATOM
     ATOM
             41 O HOH 541
                              43.310 1.560 41.912 1.00 43.56
                                                             HOH
     END
```

FIG.1

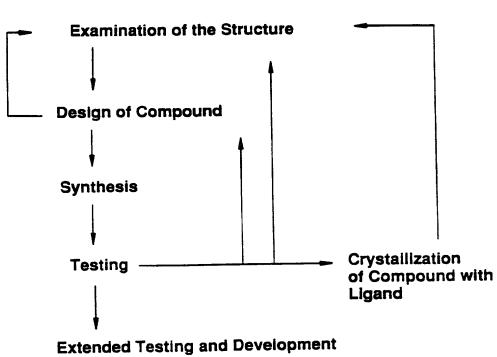


FIG.2

DOMAINS : NH	2- TERMINAL	DNA BINDING	LIGAND BINDING
HOMOLOGY:	Hypervariable	> 40%	About 20%
FUNCTION: 1	Fransactivation	DNA Binding Dimerization	LIGAND Binding Dimerization Transactivation Nuclear translocation Hsp binding

09	•	•	•	•	•	•	•	•	•	•	•	•	TPTST.DGLLF	VSCVSGAIPN	•
	•	•	•	•	•	•	•	•	•	•	•	•	T ROUTED TO T		•
			•	•	•	•	•	•	•	•	•	•			•
	•	•	•	•	•	• • • • • • • • • • • • • • • • • • • •	•	•	•	•	•	•			•
	• • • • • • • • • • • • • • • • • • • •	•	•	•	•	•	•	•	•	•	•			APHVAGGPPS PEVGSFLLCK SLPEGLDMER RWGQVSQAVE	•
	•	•	•	•	•	•	•	•	•	•	•	•		MTELKAKGPR METKGYH	•
	rTRalpha	hTRalpha	hTRbeta	hRARalpha	hRARgamma	hRXRalpha	hRXRbeta	hPPARalpha	hPPARbeta	hPPARgamma	hvdr	her	hGR	hPR hMR	hAR

120	•	•	•	•	• • • • • • • • • • • • • • • • • • • •	• • • • • • • • • • • • • • • • • • • •	• • • • • • • • • • • • • • • • • • • •	•	• • • • • • • • •	• • • • • • • • • • • • • • • • • • • •	• • • • • • • • • • • • • • • • • • • •		VMDFYKTLRG	LDSVLDTLLA	YHDSVRDADY	•
	•	•	•	•	•	•	•	•	•	•	•		SSVLAQERGD		SATVAESHGL	•
	•	•	•	•	•	•	•	•	•	•	•	•	SLTPGREENP	EATRGAGGSS	IKTELESKEL	•
	•	•	•	•	•	•	•	•	•	•	•	•	MDSKE	SDVEGAYSRA	NNRPGILTSD	•
	•	•	•	•	•	•	•	•	•	•	•	•	•	PCOGODPS DEKTQDQQSL	TOGSSKEK QELLPCLOQD	•
61	•	•	•	•	•	•	•	•	•	•	•	•	•	PRPCOGODPS	NSTOGSSKEK	•
	rTRalpha	hTRalpha	hTRbeta	hRARalpha	hRARgamma	hRXRalpha	hRXRbeta	PPARalpha	hPPARbeta	1PPARgamma	hVDR	her	hGR	hPR	hMR	har

FIG.38

180	•	:	:	•	•	•	•	•	•	•	:	:	4	\$	Ö	•
7	•	٠	•	:	:	•	:	:	:	:	:	•	DFPKGSVSNA	GI	SDSGSSVNGG	•
	:	•	•	•	•	:	•	•	•	•	:	•	SS	SS	SS	:
	•	•	•	•	:	•	•	•	•	:	•	•	PK	ဌ	SG	•
	•	•	•	•	•	:	:	:	•	•	•	•	DE	LSPLMSRSGC KVGDSSGTAA		•
	•	•	•	•	•	•	•	•	:	•	•	•	.DSKQRRLLV	ပ္ပ	NTPLRSFH	•
	•	•	•	•	•	:	•	•	•	•	:	•	R	RS	RS	•
	•	:	•	•	•	:	•	•	:	•	:	•	S S	,XS	:	•
	:	•	•	•	•	•	•	•	•	•	•	•	SX	PI	IPI	:
	:	:	•	:	:	:	•	:	:	:	:	:	-			:
	:	:	•	•	•	:	•	•	:	•	•	•	•	<b>PPAAPATORV</b>	GHRPSTLSCV	:
	:	•	:	•		:		•	•	•	•	•	•	TO	LS	•
	:	•	:	•	:	•	:	:	•	•	•	•	•	PA	ST	•
	•	•	•	•	•	•	•	•	:	:	:	•	•	Z	IRP	:
	•	:	•	:	•	:	•	•	•	•	•	•	•	<u>04</u>	CH	•
	•	•	•	•	•	•	•	•	•	•	•	•	•	G	N	:
	•	•	:	•	:	•	:	:	•	:	•	:	•	14.7	X	•
	:	:	:	:	:	:	:	:	:				•	E	Ŧ	
	:	:	:		•			:		:	•	•		FG	5	•
	•	•	•	•	•	•	•	•	•	•	•	:	•	CLFGPELPED	EQLVKFYKGN	:
		•		•	••.		•	•	•	•	•	•		PPACEVTSSW	MSPAKIYQNV	•
	•	:	:	•	:	•	:	•	•	:	•	•	SQ	SS	Ö	•
	:	•	•	•	•	•	•	•	•	:	:	•	IAS	\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	I X	•
	•	•	•	•	•	:	•	•	•	:	•	:	4	S	¥	•
	•	•	:	•	•	•	•	•	•	•	•	•	PSLAVASQS.	dd	4SE	:
	•	•			•	•	•		•	•	•		S	S	S	•
	:	:	•	•		:		•	•	•	•	•	<b>FVKVSASS</b>	PSGPGQSQPS	EQQNQQGS	•
			•	•	•	•	:	•	•	:	:	•	VS	OS	ğ	•
	•	•	:	•	•	•	•	•	•	•	•	•	X	PG	8	•
121	•	•	•	:	•	•	•	•	:	•	•	•	GAT	SG	SYE	•
Н	•	•	٠	•	•	•	•	•	•	•	•	•	G	Ωı	S	•
	la	ıa	rd	Ja	Ja	Ja	6	פו	ď	שו	)R	her	hGR	hPR	<b>hMR</b>	<b>hAR</b>
	rTRalpha	hTRalpha	hTRbeta	hRARal pha	hRARgamma	hRXRalpha	hRXRbeta	td.	hPPARbeta	E	hVDR	hE	Ъ	h	之	'n
	la]	[a]	2	a]	ζgë	a]	(R.	{a}	K	ζģέ	_					
	TH	TH	hī	₹.	\$	X	5	AF	PP	AF						
	H	-		h	h	Z		hPPARalpha	ΡÏ	hPPARgamma						

-16.3C

ESAGPLLKGK

hGR hPR

P. W.

hvdr her

hPPARgamma

hPPARbeta

ESIANLNRS.

240

181

hTRbeta

hRARalpha hRARgamma hRXRalpha hRXRbeta hPPARalpha

hTRalpha

rTRalpha

SSTIASFGSF PVHSPITQGT SGETDLKLLE VEEEDSSESE VCSPAGINSV KPSPQAAAVE FPQQCQISLS FIG.3D VCSPLNHTSS ETKVMGNDLG ESPHWSGAPV PIMCHEKSPS LSHGLYHGET PARQLLLPAS QQPDLSKAVS AHKVLPRGLS VHRAIVK..S

6/50 300 ALVEQDAPMA PGRSPLATTV SPPSHCSVKS PVSSPNNVTL HLKGQTGTNG GNVKLYTT. THSDVSSEQQ EDSRFSAPRV PLSSHKSSIS ASNVGSPLSS AAPTEKEFPK AAGGVALVPK GGAAACPPGA RGSRSHSPAH PKSSASTAVS PLTCSPNAEN ...TSVPEN PRALGGRAAG 241 hvdr her hgr hPR **h**HR hPPARgamma hRARgamma hPPARalpha hPPARbeta hTRalpha hRARalpha hRXRalpha hRXRbeta rTRalpha hTRbeta

-16.3E

	301					360
rTRalpha	•	•	•	•	•	•
hTRalpha	•	•	•	•	•	•
hTRbeta	•	•	•	•	•	•
hRARalpha	•		•	•	•	•
hRARgamma	•	•	•	•	•	•
hRXRalpha	•	•	•	•	•	•
hRXRbeta	•	•	•	•	•	•
hPPARalpha	•	•	•	•	•	• • • • • • • • • • • • • • • • • • • •
hPPARbeta	•	•	•	•	•	•
hPPARgamma	•	•	•	•	•	• • • • • • • • • • • • • • • • • • • •
hvdr	•	•	•	•	•	•
her	•	•	•	•	•	
hGR	•	DQST	FDILQDLEFS	SGSPGK	ET	NESPWRSDLL
hPR	MDFIHVPILP	LNHALLAART	RQLLEDESYD		SA	FAPPRISPCA
h HR	RSSVSSPANI	NNSRCSVSSP	SNTNNRSTLS	SPAASTVGSI	CSPVNNAFSY	TASGISAGSS
har	•	•	•	•	•	•

FIG.3F

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		•	•	•		
AARPPFLPOR HAEGSVGKWG		MSH	•			
	•	•	•	:		
	:	•	•	•		
• • • • • • • • • • • • • • • • • • • •	•	•	•	:	•	
• • • • • • • • • • • • • • • • • • • •	•		•	:	•	
WIW	•	•	•	•	•	• • • • • • • • • • • • • • • • • • • •
DNGDLVLSSP SNVTLPQVKT		ILPDTKPKIK		NEDC	SFLLE GNSNEDCKPL	AGEDDSFLLE GNSNEDC
IKEEEEGAEA SARSPRSYLV		YSDFOPPALK		KDDA	SAYPPD AEPKDDAYPL	
TWOVIKPEPD GAFSSSCIGG						
		TONCATORET		ASSI	AQEVP FPKTEEVESA	TOEKGAQEVP FPKTEEV
	•	• • • • • • • • • • • • • • • • • • • •	:	•	• • • • • • • • • • • • • • • • • • • •	• • • • • • • • • • • • • • • • • • • •

FIG.3G

480 MSAISVHGVS **PASASVSSAS** KDYYSLSGIL SRSPDSSSPN YPEGAAYEFN TIRVLEVEVD VAPYGYTRP. FSTQVNSS. ....GA .....AA SVPIKQESTK HSCSGISFKG NPTVNPFPFM DGSYFSFMDD PLERPLGEVY LDSSKPAVYN XX.... HDTKHFLPLD SCILKFPAQD AQVIVMSGQE RDGRH..GRD PGAGARGWTG ANIIG.... PR.ATPSRPG EAAVT.... .....GG GGGEA.... TVYCQASFPG EPLNRPQLKI GGGGRRRITN PLTVNEQLLG FPLGPPPPLP ALAGSRSGGG PGVIKQEKLG DTEDLPANNA LLHQIQGNEL AGANPAAFPD AKECIVGSAT EKEDFIELCT NSKINSDSSF **X**::: TLHTKASGMA 421 **h**HR hvdr her hGR hPR HAR hPPARbeta hPPARgamma hRXRbeta nPPARalpha rTRalpha hTRalpha hTRbeta hRARa 1pha hRARg amma hRXRalpha

# FIG.3H

	481					7
rTRalpha	• • • • • • • • • • • • • • • • • • • •	•		•	MEQKPSK VECGSDPEEN	VECGSDPEEN
hTRalpha	•	•	•	•	HEQKPSK VECGSDPEEN	VECCSDPEEN
hTRbeta	•	•	MTPNSHTE	NGLTAWDKPK	HCPDREHDWK LVGHSEACLH	LVGHSEACLH
hRARalpha	• • • • • • • • • • • • • • • • • • • •	•	•	•	•	•
hRARgamma	•	•	•	M AINKERLFAA GALGPGSGYP	ATNKERLFAA	GALGPGSGYP
hRXRalpha	.LTSPIGR	GSMAAPSLHP	SLGPGIGSPG	.QLHSPISTL	SSPINGHGPP FSVISSPHGP	FSVISSPHGP
hRXRbeta	PLPQGVPP	PSPPGPPLPP	STAPTLGGSG	APPPP	PMPPPPLGSP	FPVISSSHGS
PPARalpha	HVDTESPL	CPLSPLEAGD LESPLSEEFL	LESPLSEEFL	QEMGNIQEIS QSIGEDSSGS	QSIGEDSSGS	FGFTEYQYLG
hPPARbeta		MEQPQ	EEAP	EVREEEEKE	EVREEEEKE EVAEAEGAPE INGGPQHALP	LNGCPQHALP
PPARGamma	•	MVD.	TEMPFWPTNF	GISSVD	LSMMDDHSHS FDIKPFTTVD	FDIKPFTTVD
hVDR	TALSSAGAAE		SLEATEEAQL	DGPVTTSSTT	AUTVEVSAPV VQTVVSKAAI	VQTVVSKAAI
her	AAAAANAQVY		SEAAAFGSNG	LGGFPPLNSV	SPSPLMLHP PPQLSPFLQP	PPQLSPFLQP
hGR	TSGGQHYHYD	HNTASLSQQQ	DQ	KPIFNVIPP IPVGSEN.	IPVGSEN	•
hPR	SSGSTLECIL	YKAEGAPPQQ	GPFAPPPCKA	PGASGCLLPR DGLPSTS	DGLPSTS	•
hHR	GPPVPGFDGN	PVPGFDGN CEGSGFPVGI KQEPDDGSYY PEASIPSSAI VGVNSGGQSF	KQEPDDGSYY	PEASIPSSAI	<b>VGVNSGGQSF</b>	HYRIGAQCTI
hAR	•		SDFTAPDVWY	PGGHVSR	VPYPSPT	•

## FIG. 3

009	SGYI	SGXI	TEEKKCKGYI	EEIVPSPPSP	<b>EEHVPSSPSP</b>	VLKVPAHPSG	GLHCPPPPGG	YPWVPGSVDE	DOLOHGC. DG	AOLYNRPHEE	A CSVGGOGGT.	DECEMBER A	TSSSSGGS5	. SSFFSSSS	DSEASQSFQI	VSSSTLRSVS	•	
	•	•	<b>QSVSSAQTFQ TEEKKCKGYI</b>	AAIETQSSSS	LSVETQSTSS	DIKPPLGLNG	DVKPPVLGVR	SSPS. SVT	SCPP SLL DOLOHGC.DG	NACODYCE K	FASE LISEN	GOPLLIFLSA	GGRERLASIN	· · · · · · · · · · · · · · · · · · ·	YPPYLNYLRP	YPVLEYIPEN	T.P. IDYYFP	
	•	•	FHLDHDDVND	SNHVASGAGE	OPDLPKEHAS	PHNPVSSSE	T PGGGSGPPE		•		QEYQSAIRVE	TCHLAQQSSL	YRPNSDNRRQ	GYSSPSMRPD	AVLKEGLPQV	GDLSSRRSDG	VPT STABUHV	- Serence
	LKSSH		LIOTTWISSI	PN SNHVASGAGE AAIETQSSSS	MI SPSFRGIG	GENOTICS PHINPVSSSE DIKPPLGING VLKVPAHPSG	SCHOOLS TENSING TENSING TENSING SCHOPPEGG	SSECTIONS TO SECTION SOLD APPROPRIES	•		VADYKYDLKL	LTQDGLASLH TGMLAQQSSL GQFLLIFLSH AGSTGGGGG	AGPPAF YRPNSDNRRQ GGREKLASIN DAGSTALLESA	NFPGRTVFSN	NGLPOLGYQA	NTLVESWKSH		7517
			TKN FOSSPH	, , , , , , , , , , , , , , , , , , ,	THE STATE OF DEPT. MI SPAFREIG OPDIPKEMAS LSVETOSISS EEHVPSSPSP	ALK.GSEFFE	TIPITEST.		TDTLSPA	LSRS	DIPFTRADPH VADYKYDLKL QEYQSAINVE FASFIISEN METHORMAN	PITVQACPQV	HGQQVPYYLE NEPSGYTVRE	RCOGSG DDNLTSLGTL NFPGRIVFSN GYSSPSMRPD V		CARABBOOK BOHI KERPPV NILVESHKSH GDLSSRRSDG YPVLEYIPEN VSSSTLRSVS	SACAMANA EXILEMENT OF THE MAN ADDRESS OF THE TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOTAL TOT	WMDSYSG
•	541 CARSPUCKRK RKN.GOCP	CAPABLE BOOK BKN. GOCS.	SALES SERVICES TO FOSSPH LIOTTWISSI FHLDHDDVND	Kashserasi		GAGFFFAFFG			SCPGSDGSVI	SSSYTD	FSSISAPHYE	SVSPAQQTSV	HGQQVPYYLE	WNRCOGSG	a Dada a a a	ASARAGA POOS	STOROUGH	CVKSEMGP
		rikaipua	nikalpua.	hTKDeta	hRARalpha	hRARgamma	hRXRalpha	hRXRbeta	hPPARalpha	hpparbeta	hPPARgamma	hvdr	her	804 804	2011	nPR.	P. P. P. P. P. P. P. P. P. P. P. P. P. P	DRA

## FIG.3.

099 QAVLQPQHSA DR. PSYLDKDEQC VVCGDKATGY HYRCITCEGC KGFFRRTIQK NLHPTYSCKY KLVYD...KC KLEYE...KC NM.. VYTCHR KLIYD...RC SVQTQLQAPA HN. DYMCPA NM..VYTCHR DL..TYTCRD DL..TYSCRD **QHNYLCAGRN** QHNYLCAGRN HYGALICGSC KVFFKRAAEG KQKYLCASRN NLHPTYSCKY NLHPSYSCKY **QHNYLCAGRN** HYGUVICGSC KVFFKRAVEG KGFFRRTIRM AGLQAATVLN KAFFKRSIQG KVFFKRAVEG HYGVLTCGSC KVFFKRAMEG KGFFRATIOK KGFFRRTIQK KGFFRRSIQK KGFFRRSIQK KGFFKRTVRK KGFFRRTIRL KGFFRRTIRL KGFFKRTIRK HYGVLTCGSC FVCQDKSSGY HYGVSACEGC AICGDRSSGK HYGVYSCEGC AICGDRSSGK HYGVYSCEGC HYGVHACEGC HYRCITCEGC HYRCITCEGC HYGVSSCEGC HYGVHACEGC HYGVHACEGC HYGVWSCEGC PAGGLLKLPF LVCGDEASGC LICGDEASGC LICGDKASGC VVCGDKATGY WCGDKATGY **FVCNDKSSGY** RICGDKASGY LVCSDEASGC RVCGDKASGF RVCGDKASGF ATLPGLAAAS AVCNDYASGY SFESLPOKIC TGSSRPSKIC SPSGALNIEC ASCGSLNMEC PSNSLMAIEC .... POKTC PSYLDKDELC PPLPRIYKPC PPPPRVYKPC NHASFTKHIC PGAG. . KRLC KET...RYC ATTGPPPKLC PSYLDKDEQC AVLTLPTATV hGR hvdr her hPR HAR H hRARgamma hRXRbeta hPPARbeta rTRalpha hTRalpha hTRbeta hRARalpha hRXRalpha hPPARalpha hPPARgamma

## FIG. 3K

_				_		_	_							_	<b></b>	
07/	EEMIR.	. EEHIR	. EELQK	. EVPKP	.EVKEE	.STSSA	. CAGGA	.EILTC	.GLTAN	EI.SS	ISSLTT	. GEVGS	.QATT.	. ALDAV	. EEQPQ	. EGEAS
	RRK.	RRK.	RRR.	KKK.	KKK.	EVE.	DCE.	LKA.	LVA.	LLA.	QPQF	EGR.	GIQ.	WR.	GIH.	LQE.
	RKL I EQNRER	VLDDSKRVAK RKLIEGNRER RRKEEMIR	RKL I EENREK	RNK KKKEVPKP	RNK KKKEVKEE	KDRNEN EVESTSSA	KDK. DG DGE CAGGA	. RMPRSEKAK LKA EILTC	.RMPEAEKRK LVAGLTAN	.RHPQAEKEK LLAEI.SS	AIISAASLGA QPQFISSLTT	LKHKRQRDDG	RKTKKKIK GIQQAIT.	RKFKKFNKVR VVRALDAV	RKSKKLGKLK GIH EEQPQ	RKLKKLGNLK LQEEGEAS
	VLDDSKRVAK	VLDDSKRVAK	VLDDSKRLAK	VRND	VRND	VQEERQRG	VQEERQRG	IRFG	IRFG	IRFG	LQTAGLSINP	IRKDRRGGRM	•	•	•	•
	CIAVGMAMDL	CIAVGHAMDL	CIYVGHATDL	CFEVGMSKES	CFEVGMSKEA	CLAHGHKREA	CLATGHKREA	CLSVGMSHNA	CLALGMSHNA	CLAVGMSHNA	ASEPSVSVAT	CYEVGHHKGG	CLQAGMNLEA	CCQAGMVLGG	CLQAGMNLGA	CYEAGHTLGA
	IDKITR NQCQLCRFKK CIAVGHAMDL VLDDSKRVAK RKLIEQNRER RRKEEMIR	IDKITR NOCOLCRFKK CIAVGHAMDL	IDKVTR NQCQECRFKK CIYVGHATDL VLDDSKRLAK RKLIEENREK RRREELQK	NRCQYCRLQK CFEVGMSKES VRND	NRCQYCRLQK CFEVGMSKEA VRND	IDKRQR NRCQYCRYQK CLAMGMKREA VQEERQRG	DCTVDKRQR NRCQYCRYQK CLATGHKREA VQEERQRG	IOKKNR NKCOYCRFHK CLSVGMSHNA IRFG	SCKIQKKNR NKCQYCRFQK CLALGMSHNA	NCRIHKKSR NKCOYCRFOK CLAVGMSHNA	LOAMOQTQTT AATTASIVQK ASEPSVSVAT LQTAGLSINP	OCTIDKNRR KSCQACRLRK CYEVGMHKGG IRKDRRGGRM LKHKRQRDDG EGRGEVGS	IDKIRR KNCPACRYRK CLQAGMNLEA	CIVDKIRR KNCPACRLRK CCQAGHVLGG	IDKIRR KNCPACRLQK CLQAGMNLGA	CTIDKFRR KNCPSCRLRK CYEAGHTLGA
199	. CCVIDKITR	. CCVIDKITR	. KCVIDKVTR	INKVTR	INKVTR	. DCLIDKROR	. DCTVDKRQR	. SCKIQKKNR	. SCKIQKKNR	. NCRIHKKSR	LOAMOOTOTT	OCTIDKNRR	CIIDKIRR	CIVDKIRR	CIIDKIRR	CTIDKFRR
	rTRalpha	hTRalpha	hTRbeta	hRARalpha	hRARqamma	hRXRalpha	hRXRbeta	hPPARalpha	hPPARbeta	hPPARgamma	hvdr	her	hGR	hPR	hmr	hAR

FIG.31

780	•	•	•	•	•	•	•	IHDMETLCHA	IHDIETLWQA	IYDHNSLAHG	EPA	•	LL	LL	VL	VL
	PDDIGQSPIV	PDDIGQSPIV	PEDIGQAPIV	TNNSSEQRV.	INSSADHRV.	SP	SP	GKASNNPPFV	GKASHTAPFV	GKTTDKSPFV	GAAAASA	EPPILYSE	•	•	SRALTPSPVM	•
	SHWKQRRKFL	SHWKQRRKFL	SHWKQKPKFL	CQLGKYT	CQLGKYT	GLNPSSP	GGSGSSP.	NKVKARVILS	TKKKARSILT	TKAKARAILT	PLLVNPASLA	DOMVSALLDA EPPILYSE.	PTLVS	PPLIN	TALVPQLSTI	PIFLN
	EAHRSTNAQG	EAHRSTNAOG	EAHVATNAQG	KAHQETFPAL	KAHQETFPSL	ETYVEANH	DQCVECPGGT	EAYLKNFN.H	NAYLKNFN.H	DSYIKSFP.L	NAQCQVIGTL	KNSLALSLTA	IVPATLPQLT	FSPGQDIQLI	IAPAKEPSVN	VSHIEGYECQ
F minimal start site 725	EEWDLIHVAT EAHRSTNAQG SHWKQRRKFL PDDIGQSPIV	EEWDLIHIAT	EEWELIKTVT	EVGELIEKVR	QLEELITKVS	EAELAVEPKT	EAELAVEOKS	DLKSLAKRIY EAYLKNFN.H NKVKARVILS GKASNNPPFV	DLKAFSKHIY NAYLKNFN.H TKKKARSILT GKASHTAPFV	DLRALAKHLY DSYIKSFP.L TKAKARAILT GKTTDKSPFV	VAGLTSQLIT NAQGQVIGTL PLLVNPASLA GAAAASA	PSPLMIKRSK	ETSENPGNKT	ESQALSQRFT	POSPEEGITY	STT3P TEETTQKLT VSHIEGYECQ PIFLN VL VL
	SLOCRPEPTP	SLOGRPEPTP	SIGHKPEPTD	ECSESYTLTP	GSPUSYELSP	NEDMPVERIL	PEEMPVDRIL	EDSETA	EGSQXNPQVA	DIDQLNPESA	TSAMSN	AGDHRAANLH	GVSQ	ALPOPLGVPN	ddddddd	<u>у</u>
721	SLQ	SLQ	SIG	ECS	GSP	NED	PEE	EHD	EGS	DID	TPI	AGD	•	ALP	8	STI
	rTRalpha	hTRalpha	hTRbeta	hRARalpha	hRARgamma	hRXRalpha	hRXRbeta	PPARalpha	hPPARbeta	PPARgamma	hvdr	her	hGR	hPR	hMR	hAR

FIG.3M

## FIG.3N

# FIG.30

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							17/	50								
096	LAFEHYV	LAFEHYV	LAFEHYI	EALKVYV	EALRLYA	ASLEAYC	ASLETYC	HVLRLHL	RALEFHL	QALELQL	PVLERWLAEA	DTLIHLHAKA	KELGKAIVKR	RELIKAIGLR	IPKDGLKSQA AFEEMRINYI KELRKMVTKC	KELDRIIACK
	RSGLLCVD KIEKSQEAYL LA FEHYV	RSGLLCVD KIEKSQEAYL LAFEHYV	RPGLACVE RIEKYQDSFL LA FEHYI	RQDLEQPD RVDMLQEPLL EALKVYV	RHDLEEPE KVDKLQEPLL EALRLYA	KGLSNPA EVEALREKVY ASLEAYC	EVEVLREKVY	RPGLLNVG HIEKMQEGIV HV LRLHL	RPGLMNVP RVEAIQDTIL RALEFHL	RPGLLNVK PIEDIQDNLL QALELQL	ITPKSAQKLK	HIHRVLDKIT	LFDEIRMTYI	IPLEGLRSQT QFEEMRSSYI	AFEEMRTNYI	FFDELRMNYI
	RSGLLCVD	RSGLLCVD	RPGLACVE	RQDLEQPD	RMDLEEPE		KGLSNPS	RPGLLNVG	RPGLMNVP	RPGLLNVK	SAICRFEKLD	STLKSLEEKD	VPKDGLKSQE	IPLEGLRSQT	IPKDGLKSQA	IPVDGLKNQK
	MSTD	HSTD	MSSD	icgp	ICGD	FNPDS	FNPDA	cccb	LCGD	LSGD	TATEGPAYSQ	LNSGVYTFLS	LSS	LNT	LST	FSI
	SLSAFNLDDT EVALLQAVLL MSTD	SLSAFNLDDT EVALLQAVLL HSTD	EVALLQAVLL MSSD	ETGILSAICL ICGD	ETGLLSAICL	ELGCLRAIVL	KHRDHRHDKT ELGCLRAIIL FNPDA KGLSNPS EVEVLREKVY ASLETYC	KENALELDDS DISLEVAAII CCGD	KENALELDDS DLALFIAAII LCGD	KFNALELDDS DLAIFIAVII LSGD	NFKIRRLSLG LTQTQVGQAL TATEGPAYSQ SAICRFEKLD ITPKSAQKLK PVLERWLAEA	RFRHMNLOGE EFVCLKSIIL LNSGVYTFLS STLKSLEEKD HIHRVLDKIT	ELHRLQVSYE EYLCMKTLLL LSS VPKDGLKSQE LFDEIRHTYI	EFVKLOVSOE EFLCHKVLLL LNT	OFVRLÖLTFE EYTIMKVLLL LST	EFGWLQITPQ EFLCMKALLL FSI IPVDGLKNQK FFDELRMNYI KELDRIIACK
901	SLSAFNLDDT	SLSAFNLDDT	SLSSFNLDDT	QLLPLEMDDA	QLLPLEMDDT	KHRDHQHDKT	KMRDMRMDKT	KFNALELDDS	KENALELDDS	KFNALELDDS	NFKIRRLSLG	RFRHMNLOGE	ELHRLQVSYE	EFVKLOVSOE	OFVRLQLTFE	EFGWLQITPQ
	rTRalpha	hTRalpha	hTRbeta	hRARalpha	hRARgamma	hRXRalpha	hRXRbeta	PPARalpha	hPPARbeta	PPARGamma	hvor	her	hGR	hPR	hMR	hAR

						18	/50										
0101	LFPPLFLEVF	LFPPLFLEVF	LLPPLFLEVF	M.PPLIQEML	M.PPLIREML	PIDTFLHEML	PIDTFLMEML	ALHPLLQEIY	SLHPLLQEIY	SLHPLLQEIY	EITEIAKELN	PLYDLLLEML	EFPEMLAEII	EFPEHMSEVI	<b>EFPAMLVEII</b>	DEPEMMAETT	
	NHRKHNIPHF WPKLL H KVTDLRMIGA CHASRFL H HKVEC PTE LFPPLFLEVF	WPKLLH KVTDLRMIGA CHASRFLH MKVECPTE LFPPLFLEVF	CHASRELH MKVECPIE LLPPLFLEVF	SRPHM FPKMLH KITDLRSISA KGAERVIT LKMEIPGS M.PPLIQEML	FPRML KITDLRGIST KGAERAIT LKMEIPGP M.PPLIREML	EQPGR FAKILL RIPALRSIGL KCLEHLFF FKL.IGDT PIDTFLHEML	KOKYPEQQGR FAKLLL RLPALRSIGL KCLEHLFF FKL.IGDT PIDTFLHEML	OSNHPDDIFL FPKLLQ KHADLRQLVT EHAQLVQI IKKTESDA ALHPLLQEIY	FPKLL KMADLRQLVT EHAQMMQR IKKTETET SLHPLLQEIY	FSSOL FAKVLO KMTDLRQIVT EHVQLLHV IKKTETDM SLHPLLQEIY	ET WNOKGOON LMEFVGGEPS KKRKRRTSFT POAIEVLNTY FEKNSLPTGQ EITEIAKELN	GITT COOHOR LAOLL L ILSHIRHMSN KGMEHLY S MKC.KNVV PLYDLLLEML	FGNSSONWOR FYOLT K LLDSMHEVVE NLLNYCFQTF LD. KT MSI EFPEMLAEII	FYOLT K LLDNLHDLVK QLHLYCLNTF IQSRALSV EFPEMMSEVI	EVOLT K LLDSHHDLVS DLLEFCFYTF RESHALKV EFPAHLVEII	TYCHY USV	RKNPTSCSRR FYQLTK LLDSVQPIAR ELHQFIFULL INSRMVSV DITELLIA
	CHASRFLH	CHASRFLH	CHASRFLH	KGAERVIT	KGAERAIT	KCLEHLFF	KCLEHLFF	EHAQLVQI	EHAQMMQR	EHVQLLHV	POAIEVLNTY	KGMEHLYS	NLLNYCFQTF	QLHLYCLNTF	DLLEFCFYTF	TIUDEBOUT	TTULLITUTE
	KVTDLRHIGA	KVTDLRMIGA	KVTDLRMIGA	KITDLRSISA	KITDLRGIST	RLPALRSIGL	RLPALRSIGL	KHADLRQLVT	KMADLRQLVT	KMTDLRQIVT	KKRKRRTSFT	ILSHIRHMSN	LLDSMHEVVE	LLDNLHDLVK	LLDSMHDLVS		LLDSVQPIAR
	WPKLLH	WPKLLH	HVTHF WPKLLM KVTDLRMIGA	FPKMLH	FPRMLH	FAKLLL	FAKLLL	FPKLL0	FPKLLQ	FAKVLO	LMEFVGGEPS	LAOLL	FYOLT K	FYOLT K	FYOTE		FYQLTK
1961	NHRKHNI PHF	NHRKHNIPHE	NYRKHHVTHF	RKRRPSRPHM	RRRRPSQPYM	KHKYPEQPGR	KOKYPEQQGR	OSNHPDDIFL	OANHPDAOYL	KLNHPESSOL	FI WNOKGOON	GLTLOOOHOR	FCNSSONWOR	OKGVVSSSOR	DINECOSMO	とないってどうせんと	RKNPTSCSRR
	rTRalpha	hTRalpha	hrabeta	hearalpha	hRARgamma	hRXRalpha	hRXRbeta	PPARalpha	hpparbeta		ammagare 331		נים בי מיטי	NO.		REII	har

## FIG.30

	1021	minimal end site 1025	5		1011	
rTRalpha	EDQEV	•	•	•	•	
hTRalpha	EDQEV	•	•	•	•	
hTRbeta	ED	•	•	•	•	
hRARalpha	ENSECLDILS	CQPGGGGRDG		GGLAPPPGSC SPSLSPSSNR	SSPATHSP	
hRARgamma	ENPEMFEDDS	SQPGPHPNAS	SEDEVPGGQG KGGLKSPA	KGGLKSPA	•	
hRXRalpha	EAPHQMT	•	•	•	•	
hRXRbeta	EAPHQLA	•	•			19/
PPARalpha	RDMY.	•	•	•	•	50
hPPARbeta	KDMY.	•	•	•	•	
1PPARgamma	KDLY.	•	•	•	•	
hVDR	YDREWNRVWF	CNRRQTLKNT	SKINVFQSQ.	•	•	
her	DAHRIHAPTS	RGGASVEETD	QSHLATAGST	SSHSLQKYYI	TGEAEGFPAT V	
hgR	TNOIPKYSNG	NIKKLLFHQK	•	•	•	
hPR	AAQLPKILAG	HVKPLLFHKK	•	•	•	
hmr	SDQLPKVESG	NAKPLYFHRK	•	•	•	
har	SVQVFKILSG	KVKPIYFHTQ	•	•	•	
ı						
socr:<5>						
		工	FIG.3R			

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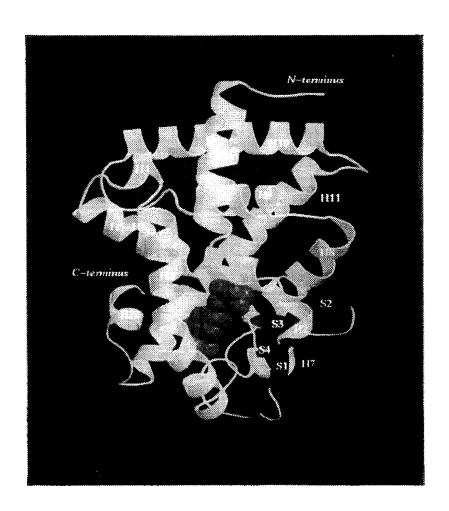
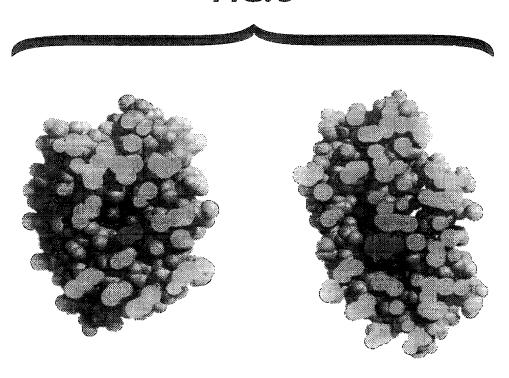


FIG.4

FIG.5



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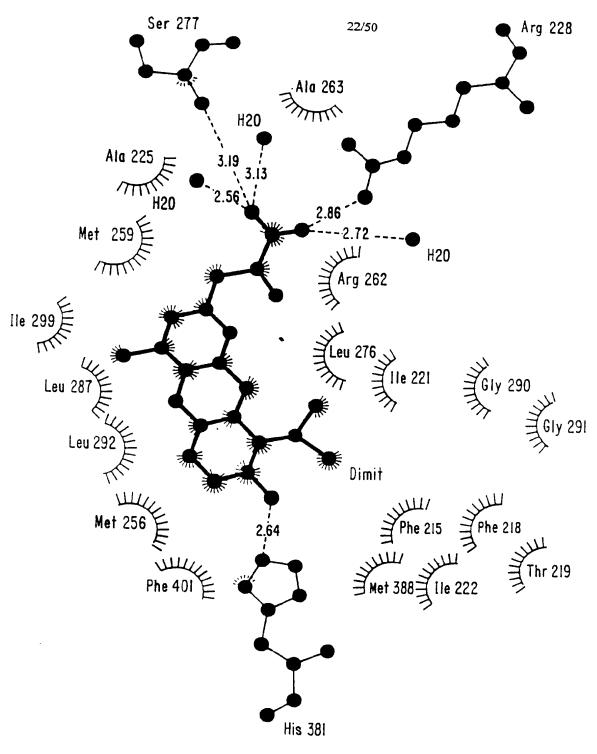


FIG.6

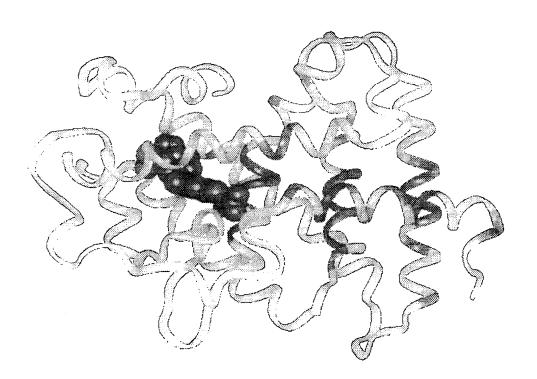


FIG.7

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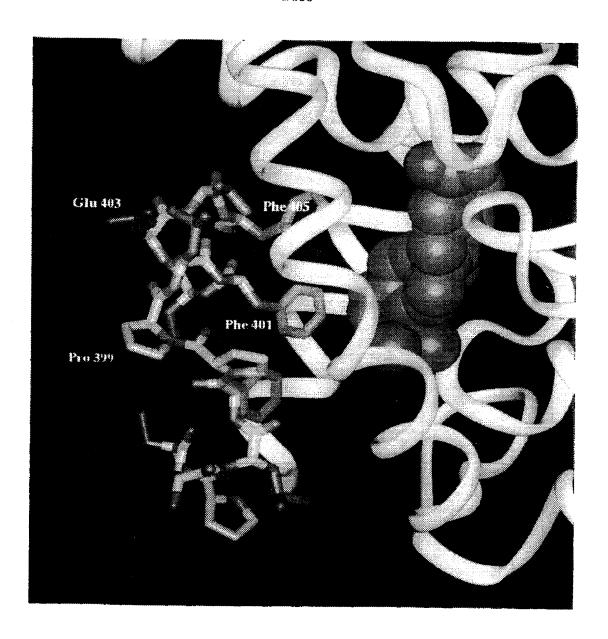
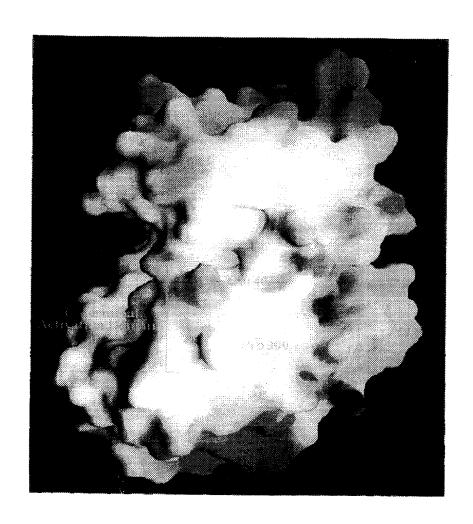


FIG.8



FG.9

### **AGONISTS**

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### **ANTAGONISTS**

Retinoic Acid

Diethylstilbestrol

Tamoxifen

Progesterone

FIG.10

shows position of extension group

Compound	RCOX
TSI	Ph2CHCO2NHS
TS2	C <sub>16</sub> H <sub>33</sub> CO <sub>2</sub> NHS
TS3 ·	FMOC-CI
TS4	tB <b>0C</b> <sub>2</sub> 0
TS5	tB0C20

FIG.11

NH2

$$CO_2H$$
 $O_2N$ 
 ### SUBSTITUTE SHEET (RULE 26)

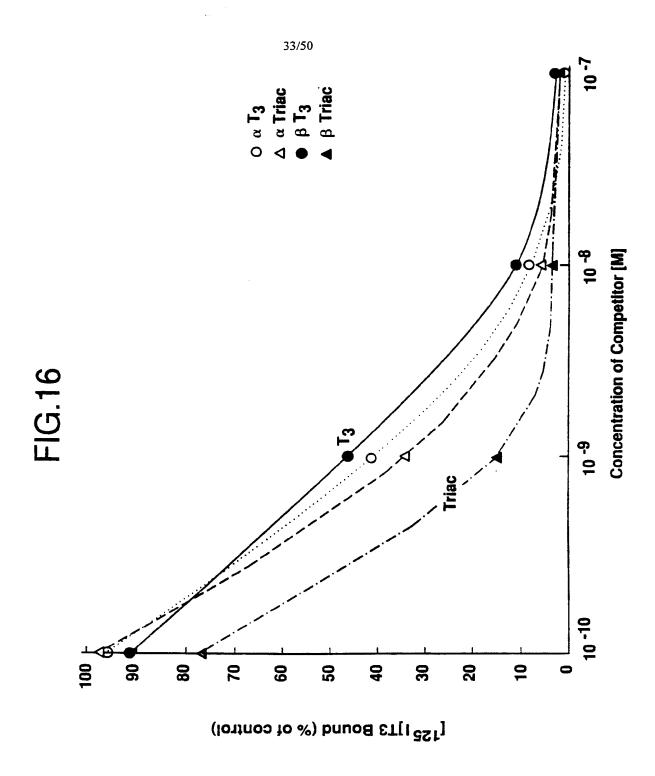
HBr, AcOH

FIG.14B

$$\begin{array}{c|c} 0 & & & \\ N & & & \\ N & & & \\ N & & & \\ N & & & \\ N & & & \\ N & & & \\ O & & & \\ \end{array}$$

### FIG.15

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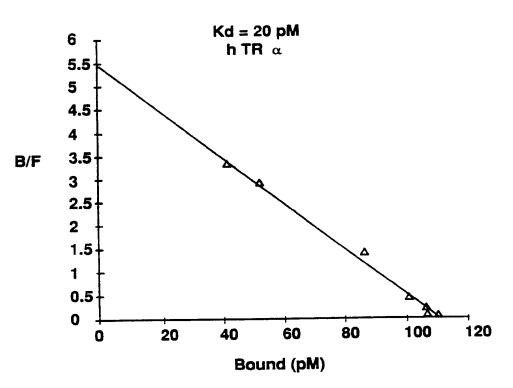
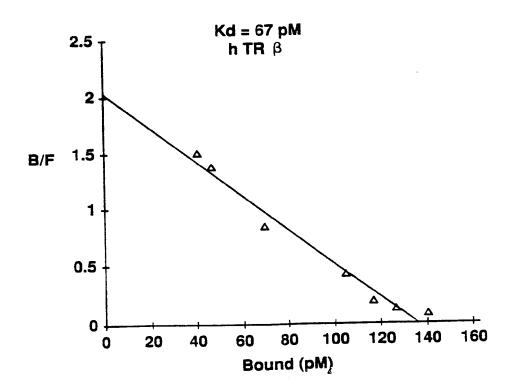
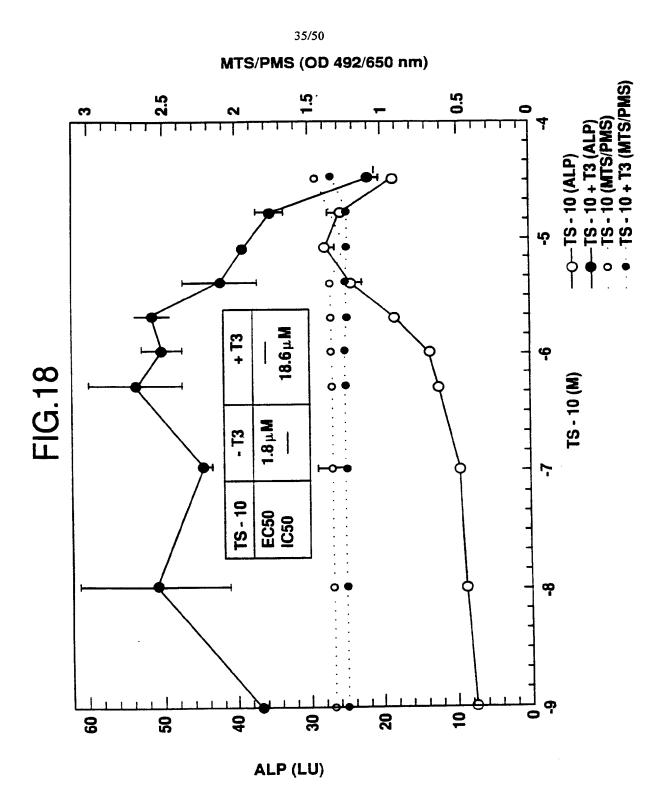


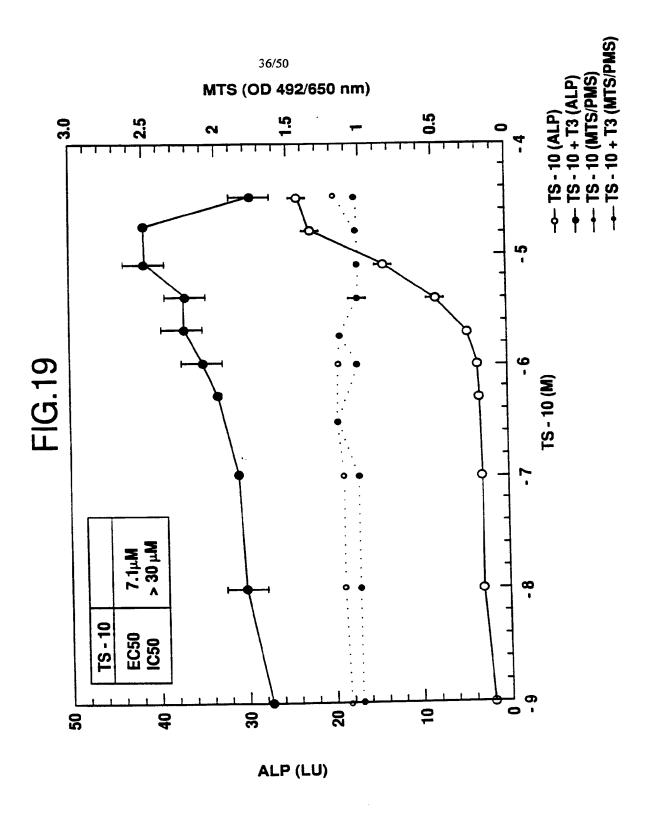
FIG.17B



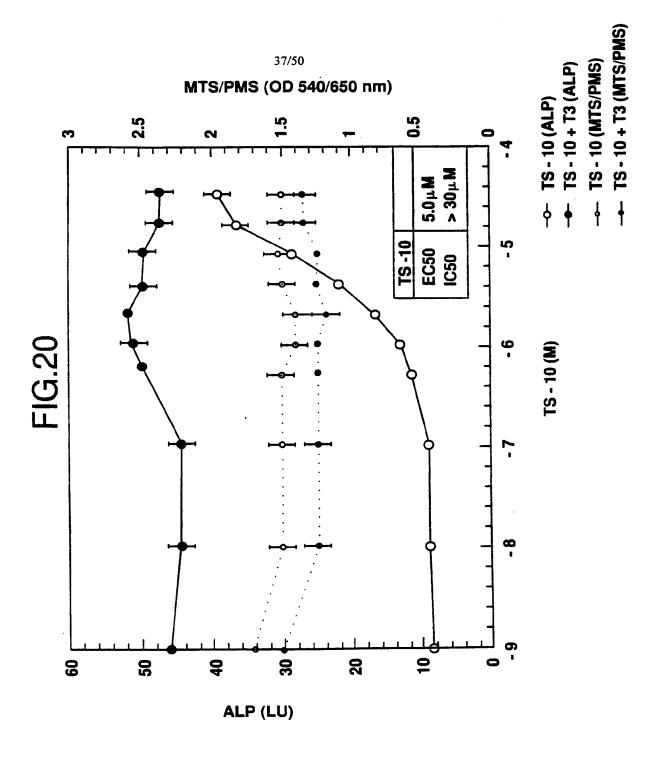
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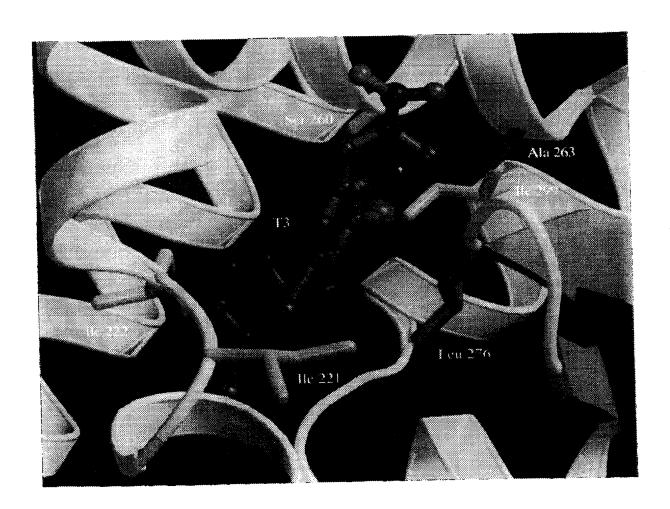


FIG. 21

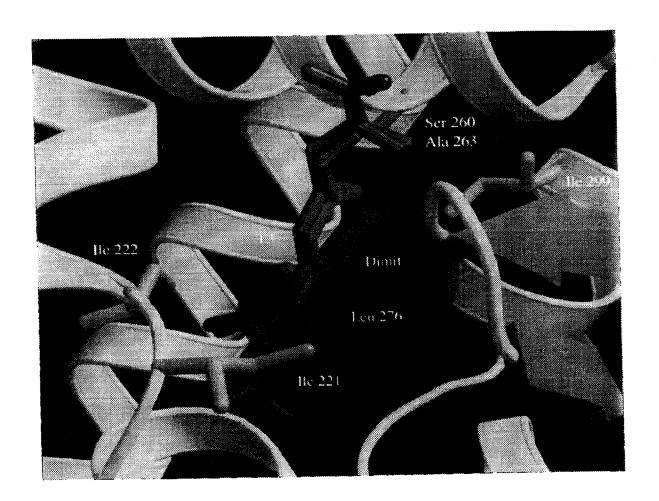


FIG. 22

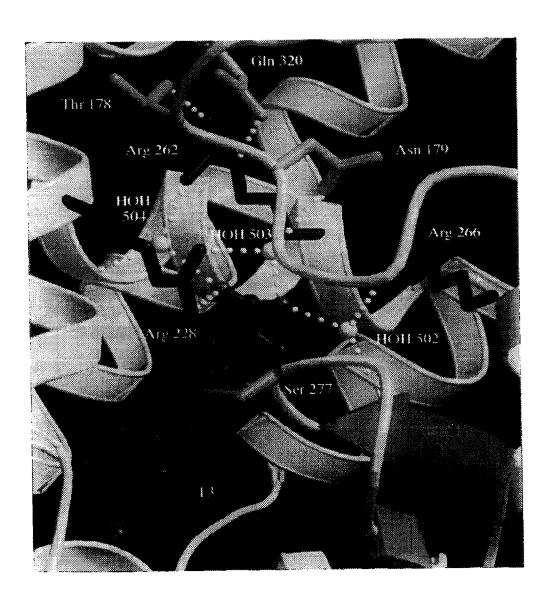


FIG. 23

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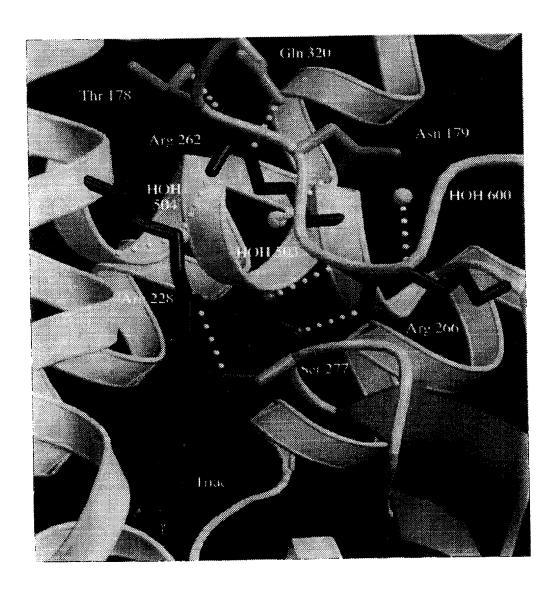


FIG. 24

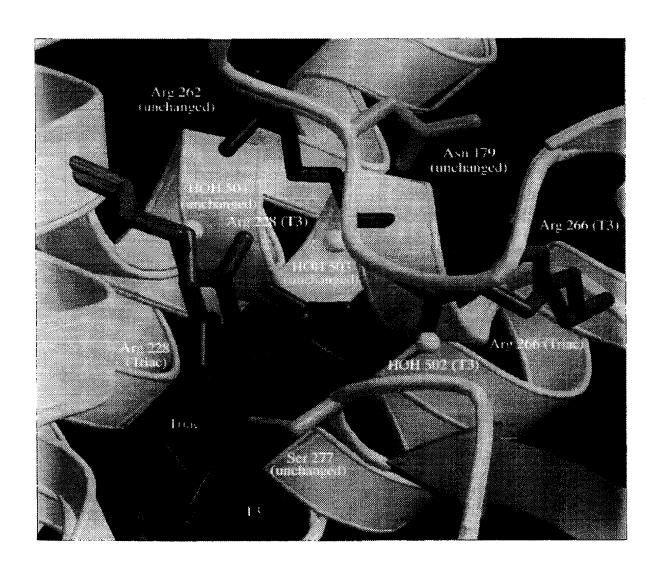


FIG. 25

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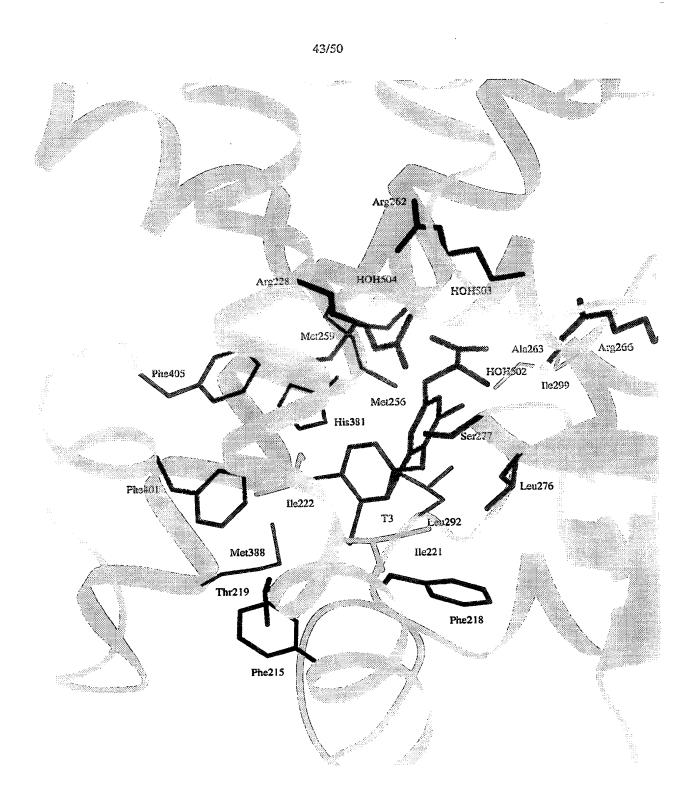


FIG. 26A

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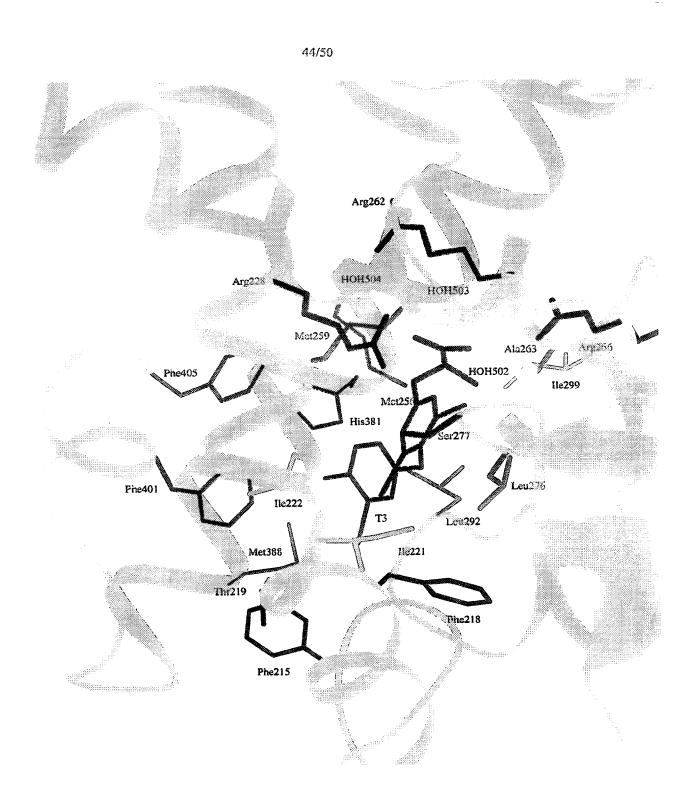


FIG. 26B

Thyroid Hormone Receptor Beta with GC1

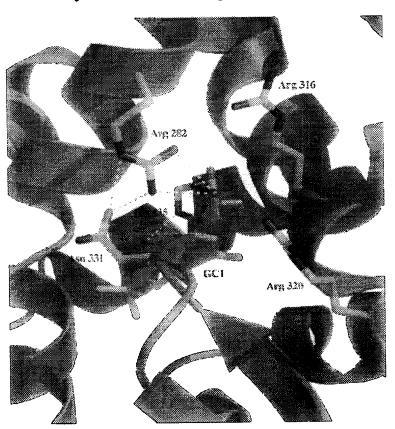


FIG. 27

Thyroid Hormone Receptor Beta with Triac

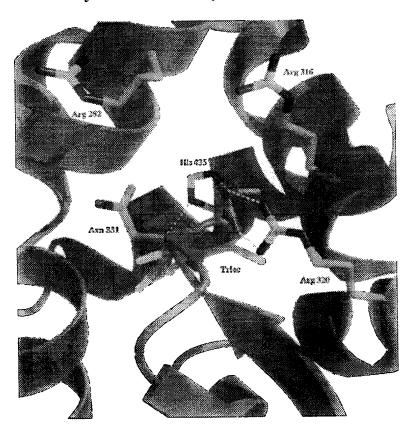


FIG. 28

## Structural Differences Between TR-b with GC1 and TR-a with Dimit



FIG. 29

## Structural Differences between TR LBD isoforms with Triac

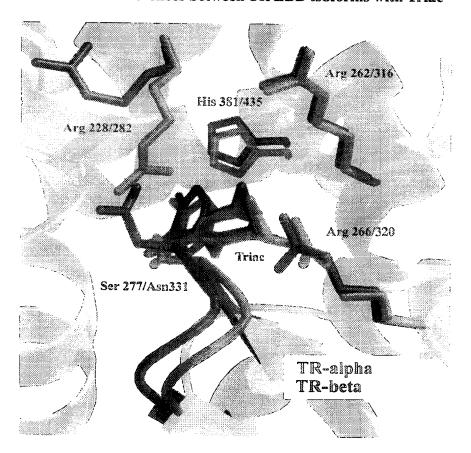
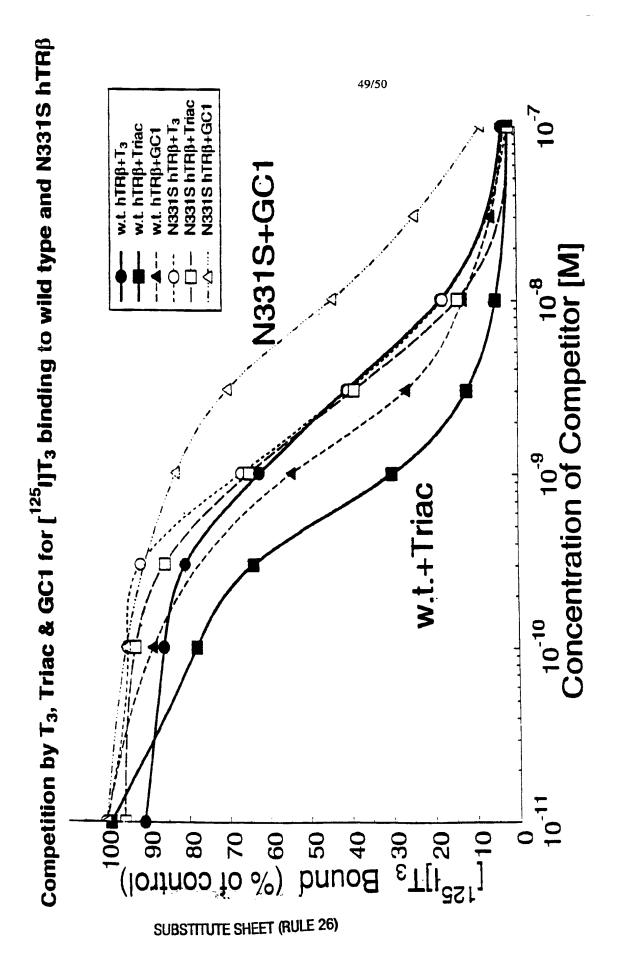


FIG. 30

**FIG.31** 



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Atomic Numbering for Thyronine-like Ligands

$$R5$$
 $C10 - C12$ 
 $C9 = C11$ 
 $R4' - C8$ 
 $C2 - X - C7$ 
 $C1 - R1$ 
 $C6 = C4$ 
 $C5 - C3$ 
 $R3'$ 
 $C5 - C3$ 

Ligand	R1	R3	R5	X	R3'	R4'
Dimit	amino propionic	C19	C20	02	iPr	01
IpBr <sub>2</sub>	amino propionic	BR1	BR2	02	iPr	<b>O</b> 1
Ť,	amino propionic	I1	13	02	12	01
Triac	acetic acid	I1	13	02	12	<b>O</b> 1
GC1	oxyacetic acid	C19	C20	C21	iPr	01

**FIG.32**